Archives of Neurology and Psychiatry

VOLUME 45 JUNE 1941 NUMBER 6

ELECTROENCEPHALOGRAPHIC CLASSIFICATION OF THE EPILEPSIES

HERBERT JASPER, D. ès Sc.

AND

JOHN KERSHMAN, M.D.

MONTREAL, CANADA

The demonstration that specific patterns of electrical discharge from the brain, recorded through the unopened skull, are related to epileptiform disorders of cerebral function has given a new approach to the diagnosis, treatment and general understanding of the nature of the epilepsies. Different forms of electrical disturbance have been found with different forms of clinical seizures, so that the electroencephalogram has given a new basis for classification. The validity and possible significance of such a classification of the epilepsies form the subject of the present report.

Gibbs, Davis and Lennox [1] first observed a characteristic form of electrogram [2] with petit mal attacks distinct from that obtained during grand mal attacks.

Later Gibbs, Gibbs and Lennox [3] discovered still another pattern of waves to characterize the electrogram during epileptic equivalent states or automatisms, which they prefer to call psychomotor attacks. These three forms of epileptic discharge are described as follows (Gibbs, Gibbs and Lennox [4]):

Grand mal is characterized by extreme acceleration of the electrical activity of the cortex; psychomotor attacks by the extreme slowing of this activity, and petit mal by the alternation of fast and slow activity. With these disorders of frequency there are also associated abnormally high amplitudes.

From the Department of Neurology and Neurosurgery of McGill University, and the Montreal Neurological Institute.

1. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133-1148 (Dec.) 1935.

2. Electrogram will be used synonymously with electroencephalogram in this report.

3. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: A Paroxysmal Cerebral Dysrhythmia, Brain **60**:377-388, 1937.

4. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy, Arch. Neurol. & Psychiat. **39**:298-314 (Feb.) 1938.

We are concerned at present not with the theoretic implications of these descriptions but merely with the validity of this classification of the epilepsies.

We have made a serious attempt to use the Gibbs-Lennox classification in routine clinical examinations of epileptic patients at the Montreal Neurological Institute. It was soon found that many of the patients who showed the typical wave and spike pattern of petit mal had major clinical seizures, or "grand mal." Major convulsions occurred also in many of the patients showing the so-called psychomotor electroencephalographic pattern, and these patients often displayed no prominent psychomotor clinical symptoms. In brief, it was found that the form of clinical seizure could not be accurately predicted from the form of the electrogram. It appeared that these patterns indicated not necessarily different kinds of clinical seizures but different kinds of cerebral disorder. The same, or similar, electrographic disorders were found even in patients not considered clinically epileptic.

Gibbs, Gibbs and Lennox have attempted to face this problem by advocating the abandonment of the term epilepsy, as known clinically, and substituting "paroxysmal cerebral dysrhythmia." [5] This disorder, diagnosed by the electroencephalogram alone, would include not only all of the epilepsies but other clinical symptoms not ordinarily recognized as epileptic. The redefinition of epilepsy in terms of the electroencephalogram may be a step in the right direction, although we consider the clinical signs of an epileptiform disorder of the brain to be as important as the electrical signs. The inconsistency in the argument of Gibbs, Gibbs and Lennox lies in the use of the clinical terms grand mal, petit mal and psychomotor to describe or designate different forms of abnormality in the *electroencephalogram,* some of which may not even be considered clinically as epileptic. Also, we believe that dysrhythmia is not the most important feature of the epileptic discharge (Jasper [6]).

Insofar as we have been able to ascertain from the literature, Gibbs, Gibbs and Lennox believe that any one of their three forms of electroencephalographic activity may or may not have a localized onset in a particular area of the brain. The wave and spike pattern of petit mal was found to arise more frequently from the frontal lobes, but not from a well restricted focus of one hemisphere. Case [7] and Case and Bucy [8] pointed out that this form of discharge is not localized, as are the random spikes.

5. Gibbs, Gibbs and Lennox (footnotes 3 and 4).

6. Jasper, H. H.: Place of Electroencephalography in Clinical Neurology: Retrospect and Prospectus, Arch. Neurol. & Psychiat. **44**:1345-1349 (Dec.) 1940.

7. Case, T. J.: Electroencephalography in the Diagnosis and Localization of Intracranial Conditions, J. Nerv. & Ment. Dis. **87**:598-602, 1938.

8. Case, T. J., and Bucy, P. C.: Localization of Cerebral Lesions by Electro-Encephalography, J. Neurophysiol. **1**:245-261, 1938.

There is still a fourth form of electrogram which has been described by Jasper and Hawke [9] as characteristic of epileptic discharges from the region of a traumatic cicatrix of the cortex. These waves were first called "sporadic spikes and slow waves" (Jasper and Hawke,[9] page 16). The "cusp-shaped spikes" mentioned by Case and Bucy [8] we shall call simply spikes, while their "saw-tooth forms" we prefer to call sharp waves.

In addition to the spikes and sharp waves obtained from local cortical lesions there are the slow or delta waves, so called by Walter.[10] "Delta wave foci" were found by Golla, Graham and Walter [11] to be prominent features of the electroencephalogram of certain epileptic patients. Sporadic or random spikes and sharp waves with delta waves constitute a pattern of discharge characteristic of focal epileptogenic lesions of the cortex. This is in contrast to the three patterns described by Gibbs, Gibbs and Lennox, which do not necessarily arise from well restricted cortical foci but seem to represent more generalized disturbances. It should be pointed out, also, that delta waves were first described as arising from local cortical lesions, such as the area adjacent to a tumor of the brain, which were not necessarily epileptogenic, so these waves cannot be considered specific for epileptic discharge.

The existing confusion concerning the relationship of the form of clinical seizure and the type of disorder in the electroencephalogram of epileptic patients has stimulated the present study—a critical analysis of the different forms of disorder in the electroencephalograms of epileptic patients and their clinical correlates.

MATERIAL

This study is based on the analysis of records from 929 electroencephalographic examinations of 494 patients with symptoms recognized clinically as epileptic. No obvious abnormality could be seen in the electrograms of 26 of these patients, that is, in about 5 per cent of the entire group. (Seven of these patients were taking phenobarbital, bromides or dilantin at the time of the examination.) Since this number represented a small percentage of the entire group, we have based our study on the 468 patients with abnormal electroencephalograms. There were 264 male and 204 female patients, and their ages ranged from 6 weeks to 69 years, with an average of 22 years.

Of the 468 patients, 282 had been admitted to the Montreal Neurological Institute for intensive study, many with the possibility of surgical therapy, and 186 were from the outpatient clinic, including a few from neighboring institutions. The nature of this group must be kept in mind in attempting to draw general

9. Jasper, H. H., and Hawke, W. A.: Electroencephalography in Localization of Seizure Waves in Epilepsy, Arch. Neurol. & Psychiat. **39**:885-901 (May) 1938.

10. Walter, W. G.: The Location of Cerebral Tumors by Electroencephalography, Lancet **2**:305-312, 1936.

11. Golla, F.; Graham, S., and Walter, W. G.: The Electroencephalogram in Epilepsy, J. Ment. Sc. **83**:137-155, 1937.

conclusions from the results of this study. It cannot be compared with a group of institutional epileptic patients. There was a certain amount of selection for focal epilepsy, because of the well known work of Dr. Penfield in this field. We feel that all forms of epilepsy were represented, inasmuch as electroencephalograms were made routinely on all patients with epilepsy who were admitted to the clinic, but probably not in the same proportions as might be found in a different, or less selected, population.

METHOD

A four channel, ink-writing electroencephalographic apparatus was used for all recordings. The patient reclined on a comfortable bed in a dimly lighted, electrically shielded, soundproofed room, with a specially trained nurse in constant attendance, who signaled all movements of the patient directly on the record. About thirty minutes of record or more was taken on each patient.

Careful localization studies were carried out in each case by the phase reversal technic. The standard electrode placements described in a previous report (Jasper, Kershman and Elvidge [12]) were used. Fourteen electrodes were applied to the heads of all patients, seven on each side, with additional ones when they were required for more accurate localization. In certain cases localization was verified from records taken directly from the dura or the pia at operation. As far as possible, records were obtained when the patient was not receiving medication.

Most examinations were carried out between clinical attacks, relatively few major clinical seizures being recorded. Since this is bound to be the case in routine examinations of patients, such an analysis should be of more value than one based on the electroencephalographic patterns taken during major seizures, records of which one is not often fortunate enough to obtain. It should be emphasized that this classification, based on interseizure records, is not directly comparable in all respects with the Gibbs-Lennox classification, which is based on the form of the electroencephalogram obtained during clinical seizures.

The electroencephalographic records alone, without reference to clinical data, were used as the sole basis of our attempts to classify electroencephalograms of epileptic patients. Only after the records of each patient were classified was reference made to all available clinical data in order to ascertain implications of the electroencephalographic records.

WAVE FORMS AND WAVE PATTERNS

Analysis of the electrograms obtained from the epileptic patients in this series revealed a wide variety of forms of disorder (figs. 1 and 2). The one outstanding feature of all records was the tendency to recurring outbursts of large voltage waves, a phenomenon which has been called paroxysmal hypersynchrony (Jasper and Nichols [13]). This was the only aspect of the records which distinguished epileptic from nonepileptic cerebral disorders. Paroxysmal excessive discharge, of any form or frequency, might be called "epileptiform," except that this again confuses electrographic and symptomatic (clinical) terminology. "Epileptic" and

12. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44**:328-350 (Aug.) 1940.

13. Jasper, H. H., and Nichols, I. C.: Electrical Signs of Cortical Function in Epilepsy and Allied Disorders, Am. J. Psychiat. **94**:835-850, 1938.

"epileptiform" are clinical concepts referring to clinical symptoms and will not be applied to the electroencephalogram.

There are various aspects of electroencephalograms from epileptic patients which might be used as a basis for classification. Division lines drawn in the present state of knowledge must be somewhat arbitrary and artificial. They must not be considered in too rigid or inflexible a sense. Among the highly varied forms and patterns, certain specific kinds of activity stand out as distinct "groups," while others seem to contain the elements of several groups.

We have mentioned the distinction between simple dysrhythmia (abnormal rhythms) and hypersynchrony (abnormally high amplitude). Another division may be made between conditions which are fairly continuous, representing a chronic state of the cerebral tissue, and those which are paroxysmal, with recurring outbursts of high voltage waves representing an acute transient condition. Another fundamental distinction can be made between disorders which are localized to a small cortical area of one hemisphere and those which appear generalized throughout all areas of the brain.

Wave forms and patterns may also be classified in other ways: They may appear irregularly, in what may be called a random sequence, with no definite periodicity or rhythm, or they may appear rhythmically, in a regular sequence.

Random Waves (fig. 1).—Paroxysmal random waves may be classified under three types according to their rapidity or duration: namely, spikes, sharp waves and slow waves.

Spikes:[14] Sporadic rapid waves or spikes appear suddenly out of the background activity at irregular intervals. They are usually about two-hundredths to three-hundredths second in duration when recorded from the surface of the scalp but appear of about one-half this duration when recorded directly from the cortex. They are comparable to the "strychnine spikes" obtained from the cortex in animals after the local application of strychnine, as demonstrated in the experiments of Dusser de Barenne and McCulloch[15] and others.

Generally spikes appear as isolated single waves of moderate or large amplitude. They may be followed by a slow wave, but the spike is primary, in contrast to the wave and spike rhythm of petit mal, in which the 3 per second wave is primary, but may often appear without the spike. Their form is independent of the cortical area from which

14. These spikes from the cortex are not to be identified with the well known spike potentials of peripheral nerves.

15. Dusser de Barenne, J. G., and McCulloch, W. S.: Some Effects of Local Strychninization on Action Potentials of the Cerebral Cortex of the Monkey, Tr. Am. Neurol. A. **62**:171, 1936.

they may be derived. They may be repeated in short trains, with quiet intervals between. Increase in frequency and amplitude and spread to wider areas mark the onset of a clinical attack.

Two slightly different patterns of spike activity may be distinguished: random spikes and multiple spikes. The random spikes usually appear as isolated single waves out of a background of normal or delta activity. The multiple spike patterns are associated with generalized rapid dysrhythmia and rapid paroxysmal rhythm (to be described later).

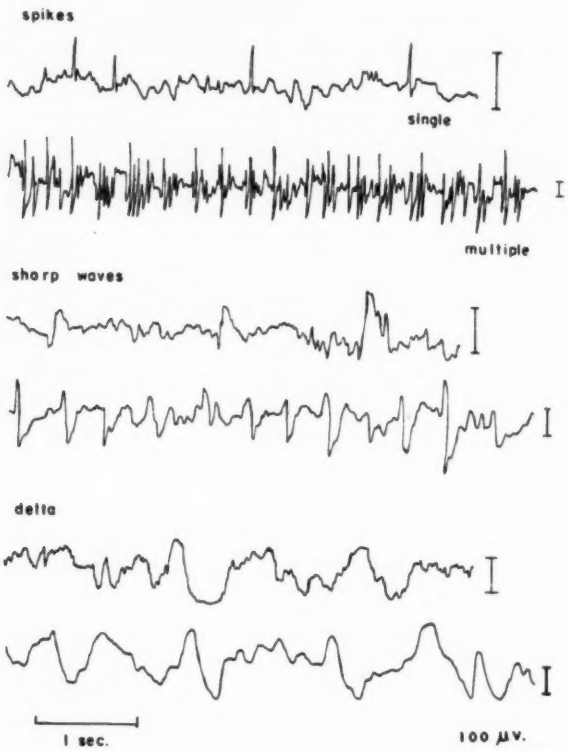


Fig. 1.—Sample electroencephalographic records from different epileptic patients to show various kinds of random waves. Two samples each of spikes, sharp waves and delta activity are given to show the tendency for an irregular rhythm to appear when waves become more frequent. These are to be contrasted with the regularity of rhythms in figure 2. All records were taken between clinical attacks. Multiple spike activity was followed by a clinical seizure in this case.

Sharp Waves: The rising phase of the sharp waves is of the same order of magnitude as that of the spikes, but the descending phase is prolonged. Repetition of these waves produces the "saw-tooth" appearance described by Case and Bucy.[8] They often appear in random sequence, in much the same way as the spikes, and are comparable in

most respects, except for their longer duration. These waves may also be reproduced in animals by applying strychnine to the cortex but appear only after more extensive (deeper) strychninization than is necessary to produce the isolated spike forms (unpublished observations). They appear to be a summation of spikes not perfectly synchronized.

Slow (Delta) Waves: Any waves having a duration of more than about fifteen-hundreds second, usually more nearly three-tenths second (equivalent frequencies being less than 7 per second), are called slow, or delta, waves if they have a smooth rather than a sharp wave front. Waves of this form were found by Walter [10] to be useful in the localization of tumors of the brain when they appear continuously from the border zone of an expanding lesion of the cortex. When such waves occur in epileptic patients they differ in two important respects: (1) They may not appear continuously but may only periodically interrupt an otherwise normal record, or (2) they may come as a sudden outburst of large voltage (paroxysmal) waves. When delta waves appear continuously at low amplitudes in records from epileptic patients, they may not have any direct relation to the epileptic discharge itself, even though they may point to cerebral tissue in the vicinity of a lesion which on occasion gives rise to paroxysmal discharge.

Paroxysmal Rhythms (fig. 2).—Certain paroxysmal discharges of the cortex tend to appear as a rhythmic sequence of waves at definite frequencies, in contrast to the random waves already described. It is true that random waves may occasionally become rhythmic, but they do not seem to have any fixed frequency. They are fundamentally sporadic, or random. In the case of the paroxysmal rhythms it is the definite frequency that is fundamental, with only a minor tendency for isolated single waves to appear.

The frequencies of these rhythms may be the same or slower than those appearing in the normal electroencephalogram. It is their hypersynchrony (high voltage) that is important. There are also certain rhythmic patterns which do not appear normally.

The most characteristic paroxysmal rhythms may be classified as follows: (1) 3 per second wave and spike patterns, (2) 3 per second waves, (3) 6 per second waves, (4) 10 per second waves, (5) 14 per second waves and (6) 25 per second waves (fig. 2).

Three per Second Wave and Spike Pattern: This is the pattern described and studied most thoroughly by Gibbs, Gibbs and Lennox.[16] It has been called the petit mal pattern because of its frequent association with this form of clinical attack.

The fundamental pattern of this rhythm is a series of regularly repeated slow waves at a definite frequency of about 3 per second. Fre-

16. Gibbs, Davis and Lennox.[1] Gibbs, Gibbs and Lennox.[3]

quencies may vary between 2 and 4 per second in different patients, and there is usually some deceleration of the rhythm toward the end of an attack.

The spikes forming a part of this pattern are comparable in form to the random spikes (or occasionally the sharp waves) already

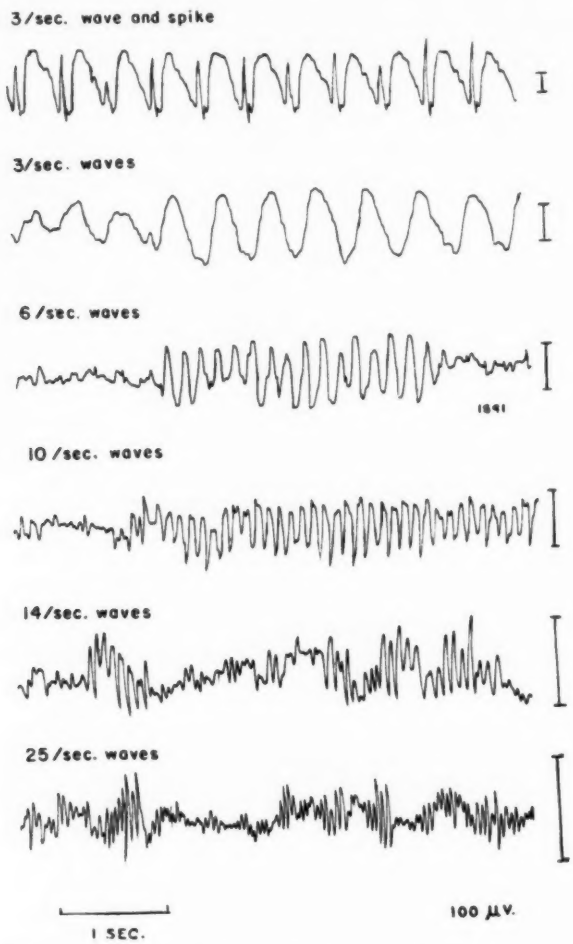


Fig. 2.—Sample records of the major forms of paroxysmal rhythm from different epileptic patients, all taken while the patients were free from gross clinical manifestation of a seizure. Note the decrease in amplitude with the increase in frequency.

described. The important difference is their subordination to the 3 per second slow wave pattern. In a given series of regular slow waves of constant amplitude the spikes may vary considerably in amplitude or even be absent completely from some of the slow waves in the series.

When they do appear they always show a constant relation in time to the slow wave, either slightly preceding it or being included in its rising or descending phase. The constancy of the 3 per second, slow wave as compared with its spike component in the wave and spike pattern is illustrated in the sample shown in figure 3.

The amplitude of this form of paroxysmal discharge varies between 100 and 1,000 microvolts as recorded with monopolar leads (surface of scalp to ear lobes). Its localization will be considered later.

Three per Second Waves: This pattern is comparable in most respects to the fundamental pattern of the wave and spike form, but each slow wave is of smoother contour (almost sinusoidal in some cases) and does not possess the spike component. These waves appear at smaller amplitudes in most patients who show the wave and spike form at larger amplitudes. Also, some patients with a 3 per second wave and spike pattern may show only 3 per second waves at lower amplitude with medication. Three cycle [17] waves might be considered simply a

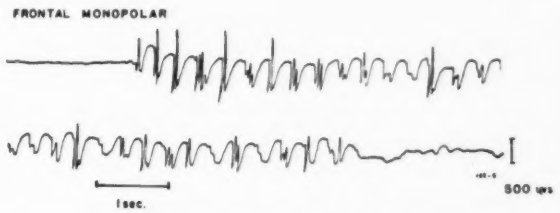


Fig. 3.—Electroencephalogram taken during a clinical attack of petit mal. Note the regularity of amplitude of 3 per second, slow waves as compared with that of spikes; yet the spikes, when they do appear, always occur at the same place in the slow wave cycle.

minor form of the wave and spike pattern, but since some patients with 3 per second waves fail to show spikes under any circumstances, the form deserves special consideration, at least for the purpose of detailed study.

Six per Second Waves: The individual waves in this regular pattern are usually rather smooth, being comparable in this respect to those of the 3 per second, slow wave pattern. Their amplitude is also comparable, or slightly less, on the average. Frequencies are fairly constant in a given patient, but vary from 5 to 7 per second in different patients. This rhythm may be associated in the same patient with a 3 cycle rhythm or in other patients with random sharp wave forms.

Ten per Second Waves: Paroxysmal 10 per second waves, with frequencies ranging between 8 and 12 per second, have not always been considered abnormal, since they are of the same frequency as the

17. "Cycle" is used synonymously with "per second" in this report.

normal alpha rhythm. For this reason they cannot be considered a "dysrhythmia." The fact that a clinical seizure may have at its onset a paroxysmal outburst of regular 10 per second waves of large amplitude proves that these waves may play a part in the epileptic discharge in some patients. Amplitudes are of the same order of magnitude as those of the 6 cycle waves. That these waves have been observed from the vicinity of certain verified epileptogenic lesions of the brain is further evidence for their inclusion in this classification. They may be associated with some random spike or sharp wave activity.

Fourteen per Second Waves: Paroxysmal rhythms at frequencies between 13 and 17 per second are included in this group. They often occur in short bursts or spindles of moderate amplitude. The background activity often consists of disorganized rapid waves or occasional random sharp wave forms, with even an occasional spike. The 14 per second waves usually appear from larger areas of the cortex than do the random wave forms. This rhythm would be included with the "grand mal" pattern of the Gibbs-Lennox classification.

Twenty-Five per Second Waves: These waves differ from the 14 per second waves only in their more rapid frequency and more usual association with an occasional spike than with sharp waves. Since the normal beta rhythm is of the same frequency as these waves, they cannot be considered a dysrhythmia. They are abnormal only when paroxysmal and of large amplitude. This rhythm would be considered among the "grand mal" forms of the Gibbs-Lennox classification.

LOCALIZATION

Localization is perhaps more important than wave form in the classification of electroencephalographic disorders of epileptic patients. From the standpoint of localization three principal kinds of activity are obtained: (1) localized (unilateral cortical), (2) bilaterally synchronous (homologous areas of the right and left hemispheres) and (3) diffuse.

Localized Discharge (*L*, fig. 4).—In certain epileptic patients the paroxysmal discharge between clinical attacks and at the onset of major attacks is always found to arise from a restricted area of one hemisphere. In cases of uncomplicated focal epilepsy the electrograms taken between clinical attacks may be normal from all regions of the head except for a small area, perhaps 3 to 4 cm. in diameter, from which occasional paroxysmal waves are recorded at irregular intervals. The onset of a clinical attack is always marked by an increase in the number and amplitude of these local discharges before they spread to other areas as the attack becomes generalized.

The form of paroxysmal wave most characteristic of a well localized epileptiform discharge is the random spike (L 1); random sharp waves

(L 2) and delta waves (L 3) are also commonly observed from local discharging areas. Occasionally local paroxysmal rhythms (L 4) of the 10 cycle or more rapid type are also observed (fig. 4). Paroxysmal rhythms, especially those with a frequency of 3 or 6 per second, readily become bilateral from homologous areas of the hemispheres, often appearing simultaneously from the two sides, while the local random waves are more commonly confined to one hemisphere. The one possible exception to this rule is that random sharp waves from one temporal lobe often have a mirror focus in the homologous region of the opposite side. The waves from the mirror focus are usually less sharp and of smaller amplitude.

Bilaterally Synchronous Activity (*B*, fig. 5).—In many patients the paroxysmal waves appear simultaneously from homologous regions of

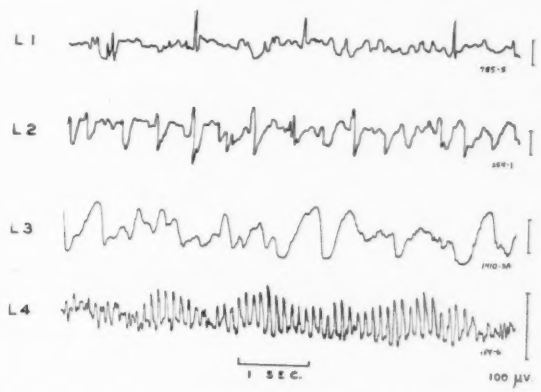


Fig. 4.—Random spikes (*L 1*), sharp waves (*L 2*) and delta waves (*L 3*) illustrate the most common forms of electroencephalograms taken from a localized, discrete superficial cortical area in patients with focal epilepsy. Paroxysmal rhythms similar to those illustrated in *L 4* are also occasionally localized.

the two hemispheres. The large voltage waves may be observed first from the frontal, the temporal or the occipital region. They might be considered localized except for the fact that the right and the left hemisphere are simultaneously involved and the waves cannot be shown to arise from a small discrete area, as do the local random spikes. Occasionally one hemisphere may appear to lead the other for a while, but often it is the opposite hemisphere that leads in subsequent examinations. Lack of consistent laterality of onset is the rule, and in many outbursts the waves appear simultaneously from the two sides.

The end of the attack is also marked by a sudden, simultaneous cessation of discharge from the two hemispheres. It is as though the two hemispheres were controlled from a common central switch, which turned them on and off together. Even more remarkable, perhaps, is

the similarity of pattern in the discharges from the two sides, the electrogram from the left side being almost a perfect mirror image of that from the right. Each wave from one side is in perfect step, synchronized with a similar wave from the opposite side. A common central (midline subcortical) pacemaker is a necessary hypothesis to account for this synchronization of bilateral discharge when there is no evidence for one hemisphere leading the other.

Paroxysmal rhythms are the most common forms of bilaterally synchronous activity. The most perfect bilateral synchrony is seen in the 3 per second wave and spike pattern (B 3 and 1), 3 per second waves (B 3) and 6 per second waves (B 4). The only random waves that show a fair bilateral synchrony are the sharp waves (B 2) from the temporal lobes, but even here they tend to become rhythmic (frequencies between 3 and 6 per second) when showing bilateral synchrony.

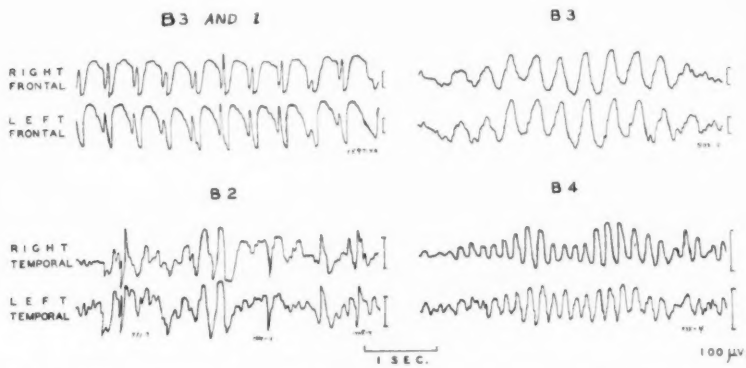


Fig. 5.—The principal forms of bilaterally synchronous activity are the wave and spike pattern (*B 3* and *1*), 3 per second waves (*B 3*), sharp waves (*B 2*) and 6 per second waves (*B 4*). Bilateral synchronous activity is obtained from homologous areas of the two hemispheres. See text for the forms of clinical seizures occurring in patients with these electroencephalographic patterns.

Diffuse, Nonlocalized Activity (*D*, fig. 6).—In a certain number of epileptic patients disorganized abnormal discharges, showing no localization to any particular area, occur from wide areas of both hemispheres and are not synchronous from the two sides. There is usually generalized disorganization of rhythms from all regions of the head. In certain cases the maximum disorder of this type may be confined to one hemisphere or may even be more marked from a large area of one hemisphere, but a discrete, well restricted focus is never observed and some generalized abnormality is always present.

Random paroxysmal waves are more common in patients with diffuse localization, although occasional rhythmic sequences are developed. They are comparable to the localized type in this respect. It is as though

there were multiple foci firing each discharge in a relatively autonomous manner, like the flashing of fireflies on a summer evening. The specific forms of this diffuse disorder may be classified in a manner similar to that given for the localized forms, namely, multiple spikes (D 1), multiple sharp waves (D 2), multiple slow waves (D 3) and paroxysmal rhythms (D 4). In the case of the localized forms similar disorders are confined to a small area of the cortex, while in case of the diffuse forms corresponding types are more widespread.

ELECTROENCEPHALOGRAPHIC CLASSIFICATION OF EPILEPTIC PATIENTS

It has been found possible with a fair degree of facility to place each of the records from the epileptic patients included in this study into the scheme of classification just described. This does not mean that only one of the types of paroxysmal disorder described was found in each

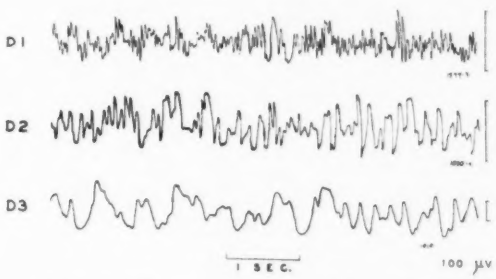


Fig. 6.—The principal diffuse patterns found in epileptic patients are multiple spikes with rapid dysrhythmia (*D 1*), multiple sharp waves (*D 2*) and multiple delta waves (*D 3*). See text for forms of clinical seizures occurring in patients with these electroencephalographic patterns.

patient. "Pure types," "textbook examples," were about as common as they are in any other diagnostic classification in medicine.

In most cases a major pattern of one type of activity was associated with a minor pattern, or subpattern, of another, usually related, form. For example, a patient with local random spikes (L 1) often had some local random delta (L 3) waves from the vicinity of the spike focus. In this case both forms of activity pointed to a localized disorder, which from the clinical point of view is of major importance. In other cases a local random spike (L 1) disorder might be combined with some diffuse delta (D 3) activity, signifying generalized abnormality in addition to the focal epileptic discharge—information of considerable importance in the guidance of therapeutic procedures.

The forms most commonly associated in the same patient are as follows: local random spikes and local delta waves (L 1 and L 3);

spikes and sharp waves, either localized (L 1 and L 2) or diffuse (D 1 and D 2); local sharp waves and local paroxysmal rhythms (L 2 and L 4); bilaterally synchronous 3 per second wave and spike activity and 3 per second waves (B 3 and 1 and B 3); bilaterally synchronous sharp waves and 6 per second waves (B 2 and B 4); bilaterally synchronous 3 per second and 6 per second waves (B 3 and B 4); diffuse multiple spikes and paroxysmal rapid rhythms (D 1 and D 4), and diffuse sharp waves and diffuse delta waves (D 2 and D 3).

It will be noted that in spite of certain combinations of specific patterns in a given patient, it is rare to find a patient who has both localized and diffuse or both localized and bilaterally synchronous or both bilaterally synchronous and diffuse disorders. Such mixtures do occur in rare cases in complex disturbances. The three major categories of localization are the most important in useful classification of the epilepsies. The specific forms and patterns are significant only in the detailed analysis of each case.

For the purpose of this study, epileptic patients were grouped according to localization and predominance of electroencephalographic patterns. Certain arbitrary standards of "predominance" were used. For example, though a patient showed fairly continuous local random delta waves and relatively few spikes, he was classified under the random spike (or L 1) type, since this form has more significance than delta waves (L 3) for epileptiform discharge. Spikes (L 1) were given precedence over sharp waves and paroxysmal rhythms (L 2 and L 4). In like manner, sharp waves were given precedence over delta waves. In the bilaterally synchronous group, the wave and spike pattern (B 3 and 1) was given precedence over the 3 cycle or 6 cycle rhythm (B 3 or B 4) when found in the same patient, because of the greater importance that can be attached to the bilaterally synchronous wave and spike pattern for epilepsy.

Diffuse spikes and diffuse sharp waves (D 1 and D 2) were given precedence over diffuse delta and diffuse paroxysmal rhythms (D 3 and D 4). With this system of classification, most patients had a dominant pattern and a subpattern. The distribution of patients according to dominant patterns is shown in the graph in figure 7.

Localized Disorder.—This form was dominant in about one half of all the patients in this series (232 of 468). In these it was mostly of the spike or the sharp wave form (89 per cent), the local random sharp wave (L 2) being the most common pattern. This does not mean that local delta activity is not common, but indicates that in epileptic patients it is usually associated with some spike or sharp wave activity, and these forms are given precedence in this classification.

Bilaterally Synchronous Discharge.—This form was dominant in 163 patients (35.5 per cent). The 3 per second wave and spike (B 3

and 1) was the most important pattern in the group, in respect both to number of patients and to distinctiveness of form. This is partly due to the precedence given this form in the classification, since 3 and 6 cycle rhythms were often found as a subpattern in patients showing the wave and spike pattern in the major discharge. There were about equal numbers of patients with sharp waves and with 6 cycle rhythms (B 2 and B 4), but again it must be noted that patients with both types were classified under sharp wave (B 2) patterns for purposes of this study.

Diffuse Disorder.—This form, with no consistent, well restricted focus of maximum discharge and little or no tendency to bilateral synchrony, was found in only 73 patients (15.5 per cent). There were equal numbers of patients showing multiple spike (D 1) and multiple

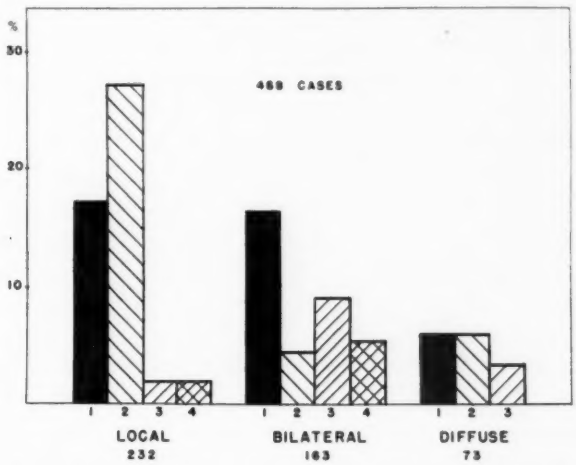


Fig. 7.—Percentage distribution of epileptic patients showing each of the different forms of electroencephalograms illustrated in the preceding figures. *LOCAL* refers to localized discharge in the electroencephalogram of (*1*) spikes, (*2*) sharp waves, (*3*) delta waves or (*4*) paroxysmal rhythms. *BILATERAL* refers to bilaterally synchronous activity of (*1*) wave and spike, (*2*) sharp wave, (*3*) 3 per second wave or (*4*) 6 per second wave forms. *DIFFUSE* refers to the generalized diffuse disorders of (*1*) multiple spikes with rapid dysrhythma, (*2*) multiple sharp waves or (*3*) multiple delta waves.

sharp wave (D 2) patterns in this group and fewer with multiple delta (D 3) patterns. Multiple delta (D 3) activity was not commonly a dominant pattern in this series of patients but was often found as a subpattern, especially in patients with multiple sharp wave (D 2) activity. Diffuse paroxysmal rhythms (D 4) were so commonly associated with diffuse spike and sharp wave forms that the pattern was not given separate treatment in this study.

ANALYSIS OF CLINICAL DATA

Seizure Patterns.—Fairly adequate descriptions of clinical seizure patterns were available, and these were corroborated by our own observations in many cases. A corps of specially trained nurses and interns at the Montreal Neurological Institute have given accurate accounts of the pattern of attacks from the onset in the cases of most patients admitted to the hospital. Detailed accounts of the form and severity of seizures were obtained from reliable observers for most of the outpatients included in this study.

Special attention has been paid to any features of the prodrome, onset or course of an attack which might serve to indicate a consistent focus of origin in a given area of the brain or the involvement of a particular set of neuronal circuits. Errors have undoubtedly crept in in considering so many varied types, but we feel that they are sufficiently few to have little influence on the main trends of our findings. The persistent attempt to discover any localizable features of the attacks has given us more information than is usually obtainable. It has also given us more cases of localized cortical seizures than could be obtained with a less detailed and extensive study of seizure patterns. Penfield's analysis of cortical localization in focal epilepsy was used throughout (Penfield [18] and Penfield and Boldrey [19]).

The forms of clinical attack were divided into four general groups: focal cortical, generalized grand mal, petit mal and psychomotor. The last three groups correspond closely to the clinical classification proposed by Gibbs and Lennox and are used here for this reason.

Patients whose attacks showed a clear focal cortical onset were placed in a separate group. Their seizures would probably be called grand mal by Gibbs and Lennox, although those of a few might be classified by them as petit mal, or even as psychomotor, when chiefly minor seizures of specific kinds were presented. The distribution of various types of seizure patterns in this group of patients is shown in figure 8.

Focal cortical seizure patterns were present in 228 patients (49 per cent). The onset in different patients included jacksonian motor attacks, adversive movements of the head and eyes, auras of any one of the sensory fields, complicated imagery or dreamy states referable to the temporal lobe and periodic aphasia resulting from local discharge in the motor speech area. Only patients with a consistently repeated pattern in each attack were included. Eighteen patients in this group (4 per cent) had, in addition to the focal cortical seizures, attacks of

18. Penfield, W. G.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449-484 (Sept.) 1936.

19. Penfield, W. G., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, Brain **60**:389-443, 1937.

epileptic automatism sufficiently marked to cause them to be included also in the psychomotor group (*psycho. focal,* fig. 8). It is important to point out that in this group the type of clinical seizure is determined by the localization of the area of onset and the course of march.

Generalized major grand mal seizures, with no consistent local onset, were present in 212 patients (45 per cent). Forty (19 per cent) of these patients had also typical petit mal attacks, and 14 (7 per cent) had on occasion what might be called psychomotor attacks or psychotic episodes. The major seizures in the majority of these patients were characterized by a sudden onset with little or no warning, usually initiated by sudden loss of consciousness and followed, or accompanied, by major convulsions with tonic and clonic components. The attacks of some of these patients were first judged to be of the focal cortical

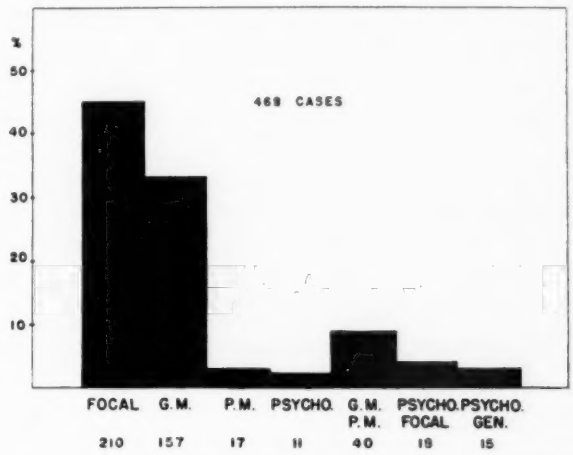


Fig. 8.—Percentage distribution of epileptic patients according to the type of clinical seizure. Those with combined types are listed separately—grand mal and petit mal (*GM., P.M.*), psychomotor and focal cortical (*PSYCHO. FOCAL*) and psychomotor and generalized grand mal (*PSYCHO. GEN.*).

type, owing to an apparent local onset in one or two attacks, but were later classified as generalized seizures because of the variability of onset in subsequent attacks. Some patients included in this group might have shown sufficient evidence of focal cortical seizures if more attacks had been observed from the onset.

Petit mal attacks of characteristic form were observed in only 57 patients (12 per cent) in this series, and 40 of these had also, on occasion, some major (grand mal) convulsive seizures. This leaves only 17 patients (3.5 per cent) with petit mal alone. Petit mal is here defined as sudden, transient loss of consciousness with little or no convulsive movement of the extremities.

Prominent psychomotor manifestations were noted in 44 patients (9 per cent). Only 11 (2.5 per cent) showed psychomotor phenomena without also being subject to occasional seizures, either of the focal cortical or of the generalized type. We have attempted to use the definition of psychomotor proposed by Gibbs, Gibbs and Lennox.

Etiologic Factors and Age of Onset.—In many cases the primary cause of epilepsy cannot be ascertained, but the principal factors apparently associated with the beginning of attacks have been studied in this series. In some cases they may represent the true cause, in others precipitating factors and in some simple coincidence.

No definite etiologic agent could be found in 211 cases, comprising 45 per cent of the total number. Hereditary factors may have been significant in a few of these cases (definite in only 12). Endocrine or metabolic disorders may have played a role in others (definite in 22), as shown by a relation to the menstrual cycle, to pituitary dysfunction or to change in carbohydrate tolerance (which was usually increased). In most of these cases the disease would be classified clinically as idiopathic or cryptogenic for purposes of a respectable expression of ignorance.[20]

Cerebral trauma due to injury to the head, either at birth or later, seemed to be an important etiologic factor in 140 cases, or about 30 per cent. This was the most important single recognized etiologic agent in this series of cases, owing partly perhaps to the degree of selection of patients sent to the Montreal Neurological Institute.

Expanding lesions of the brain, such as tumors and abscesses, accounted for the next largest group (61 cases, or 13 per cent), and vascular lesions, including cerebral thrombosis and arteriosclerosis, was the causal agent in a smaller group (21 cases, or 4.5 per cent). Infectious or toxic disease of the brain seemed related to the beginning of seizures in 35 cases (7.5 per cent).

The age of onset varied, of course, from early infancy to late adult life, depending on the nature of the etiologic agent. Seizures were first noted in the cryptogenic group usually before the age of 14 years (adolescence).

RELATION BETWEEN CLINICAL SEIZURE AND TYPE OF ELECTROENCEPHALOGRAM

There are two methods of approach to an understanding of the relationship existing between the electroencephalogram and the form of

20. "Idiopathic" or "idiopathy" is defined by Dorland (The American Illustrated Medical Dictionary, Philadelphia, W. B. Saunders Company, 1938) as a "morbid state of spontaneous origin: one neither sympathetic nor traumatic." "Cryptogenic," defined as "of obscure, doubtful, or unascertainable origin," seems more appropriate and less animistic.

clinical seizure: (1) determination of the most probable electroencephalographic findings in a patient with a given form of clinical seizure, such as focal cortical, petit mal or generalized grand mal, and (2) determination of the most probable form the clinical seizure will take in a patient with a given type of electroencephalogram, such as a bilaterally synchronous wave and spike (B 3 and 1) pattern, local random spikes (L 1) or diffuse multiple spikes (D 1).

CLASSIFICATION BY CLINICAL SEIZURE PATTERNS

Classification by the clinical seizure pattern was the method of approach used by Gibbs, Gibbs and Lennox when they derived the electroencephalographic patterns for "petit mal," "grand mal" and "psychomotor" attacks. The primary basis for these three "types of epilepsy" was the clinical seizure pattern. For example, in selecting patients with what they considered pure forms of the petit mal attack, they found a certain similarity in the electroencephalographic patterns taken during such attacks, namely, the wave and spike pattern. A similar procedure was used to determine the electroencephalographic pattern for pure grand mal and psychomotor attacks. The same procedure has been applied to our data, based on electroencephalographic records taken between clinical attacks. A fourth type has been added, namely, focal cortical seizures as determined by criteria outlined by Penfield.[18] The distribution of patients with various types of seizures according to the electrographic patterns (local, bilaterally synchronous and diffuse) which they presented is shown in figure 9.

Focal Cortical Seizures.—Most (77 per cent) of the patients with clearly focal cortical seizures as determined entirely on the basis of the form of clinical attack (localized unilateral onset and gradual march) showed localized abnormality in the electroencephalogram. The localization of the area of onset from clinical data as a rule showed a close correspondence to the localization from the electroencephalographic pattern.

In a significant proportion of patients (23 per cent) subject to seizures judged to be of the focal cortical type no consistent localization could be deduced from the electroencephalogram. It is probable that in the case of these patients there was inadequate or erroneous clinical observation or incomplete electroencephalographic study (for example, the focus may not have been active at the time of examination). In over 90 per cent of patients with sufficiently clear focal cortical seizures to merit operative exploration a corresponding focus of abnormality was found in the electroencephalogram.[21]

21. A detailed account of these studies, in collaboration with Dr. Penfield, is in preparation for later publication.

Petit Mal Attacks.—There were 57 patients (12 per cent) with petit mal clinical attacks, but only 17 who had pure petit mal, not combined with major or minor attacks of other forms (grand mal or psychomotor). Forty-eight of the 57 patients (84 per cent) showed bilaterally synchronous activity in the electroencephalogram, mostly of the wave and spike or the 3 per second wave form (B 3 and 1 or B 3).

Sixteen of the 17 patients with pure petit mal showed bilaterally synchronous activity, only 1 presenting localized sharp waves, and there was some question whether this patient had true petit mal attacks. Our findings corroborate completely those of Gibbs, Gibbs and Lennox in

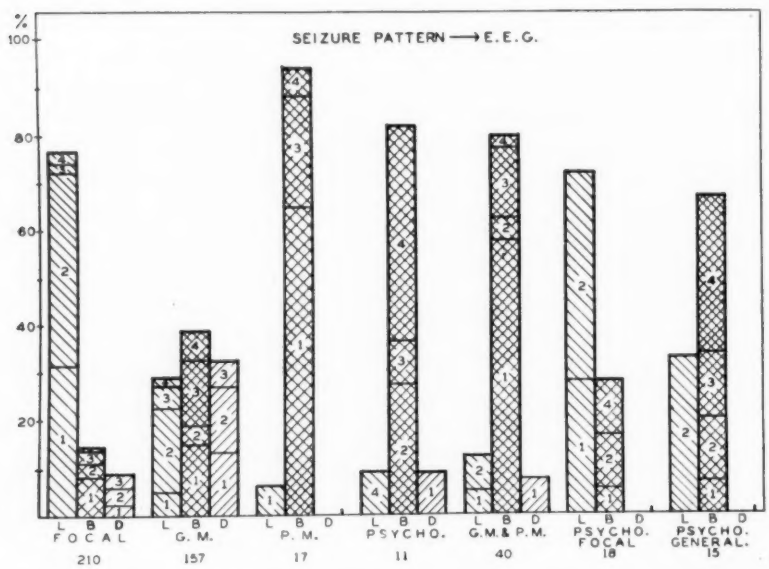


Fig. 9.—Types of electroencephalograms found in patients with different kinds of clinical seizures. Epileptic patients are grouped according to their clinical seizure patterns. Mixed patterns are listed separately. Each group is distributed separately, with the height of the columns representing the percentage of patients having localized (*L*), bilaterally synchronous (*B*) or diffuse (*D*) forms of electroencephalographic activity. The small numbers in each column refer to specific electroencephalographic patterns as previously described; e. g., *L 1* indicates random spikes; *L 2*, random sharp waves, and *B 1*, wave and spike forms. Note that most patients with the focal cortical type of clinical seizure are represented in the first column, marked *L*, with localized electroencephalographic activity. Also, those patients having only petit mal attacks clinically (*P.M.*) are nearly all represented in the *B* column, with bilaterally synchronous electroencephalographic activity, and, furthermore, their patterns are mostly the wave and spike and 3 per second wave forms (B 3 and 1 and B 3). Patients with pure psychomotor attacks only (*PSYCHO.*) have mostly the bilaterally synchronous sharp waves and 6 per second waves (B 2 and B 4).

regard to the form of electrogram obtained from patients with only pure petit mal seizures.

Grand Mal Attacks.—No characteristic electrogram was obtained from patients whose attacks were diagnosed clinically as generalized grand mal (fig. 9, *G. M.*). Of the 212 patients, 26 per cent showed localized abnormality, mostly sharp waves (L 2), in the electroencephalogram, 48.5 per cent showed bilaterally synchronous discharge, mostly wave and spike and 3 per second waves (B 3 and 1 and B 3), and 25.5 per cent showed diffuse abnormality, mostly multiple spikes and sharp waves (D 1 and D 2). Of these patients, 157 had only grand mal attacks, with no other form observed. About equal numbers of the patients with "pure" grand mal attacks showed localized (29 per cent), bilaterally synchronous (39 per cent) and diffuse (32 per cent) forms of activity in the electroencephalogram.

Psychomotor Episodes.—Pure psychomotor attacks, with only automatisms and no other form of seizure, were even more rare than pure petit mal seizures in this series of patients. A total of only 11 such patients, or 2.5 per cent, were found. Of the 11 patients, 9 showed bilaterally synchronous patterns of electrical activity, and these were of the sharp wave (B 2) or 6 per second wave (B 4) type (fig. 9). Only 1 patient was found with a right frontotemporal localized discharge, and this was also of the sharp wave and paroxysmal 6 per second wave (L 2 and L 4) form. Similar patterns were found, therefore, in practically all cases in which only psychomotor episodes occurred. The patterns here described are comparable to those called psychomotor by Gibbs and Lennox.

Patients considered clinically to have prominent epileptic equivalent states or psychomotor attacks in addition to other forms of seizure failed to show any characteristic form of electroencephalogram. For example, a patient might show typical psychomotor episodes and yet, on occasion, have a major convulsive seizure either of the generalized nonfocal or of the focal cortical type. All the various forms of electroencephalographic patterns were represented in this group of patients, composed of both "pure" and "mixed" types, though bilaterally synchronous sharp wave and 6 per second wave (B 2 and B 4) patterns were most common (fig. 9; *psycho. focal* and *psycho. general*).

Conclusion.—It appears that patients with certain "pure" forms of clinical seizures tend to show distinct forms of electroencephalogram. Patients with clearly focal cortical seizures have a localized electroencephalographic pattern, those with pure petit mal seizures the bilaterally synchronous wave and spike pattern and those with only psychomotor episodes usually sharp waves and 6 per second rhythms,

often bilaterally synchronous but sometimes localized. Patients with only clinical grand mal seizures do not seem to have a specific form of electroencephalogram when judgment is based on records taken between clinical attacks.

CLASSIFICATION BY ELECTROENCEPHALOGRAPHIC PATTERNS

The next logical step is to consider all patients with a given type of electroencephalogram, for example, all with local random spike activity (L 1), and to determine whether there is a characteristic type of clinical seizure for this group. Here we are concerned with patients classified first according to the electroencephalogram, without reference to clinical data. If the electroencephalogram is to be used in the classification of the epilepsies, as has been suggested, it is on this basis that it must be done.

It does not necessarily follow that the electrographic patterns characteristic of certain pure forms of clinical seizure, when found in a given patient between attacks, will enable one to predict accurately what kind of clinical seizures he will have. For example, the wave and spike (B 3 and 1) electrographic pattern may be found in a patient who has been observed clinically to have only major, or grand mal, seizures, even though this pattern is characteristic of clinically pure petit mal. The distribution of patients with the various types of electrographic abnormalities according to the seizure patterns they presented is shown in figure 10.

Patients with Localized Electroencephalographic Abnormalities.—Random Spike Activity (L 1): A random spike focus when well localized to one hemisphere is the most reliable electroencephalographic indication of focal cortical epileptic discharge. Seizure patterns judged clinically to be of the focal cortical type were observed in 71, or 86.5 per cent, of the 82 patients with the random spike (L 1) type of electrogram (fig. 11).

Random Sharp Wave Activity (L 2): A random sharp wave focus was slightly less reliable than a random spike focus as an indication of epileptic disorders which are recognized clinically as focal cortical in onset. There were 72.5 per cent of the 128 patients with random sharp wave activity who had clinical seizures recognized as focal cortical (fig. 11). The remainder had major seizures the clinical onset of which was not clearly of the unilateral focal cortical type and some had prominent psychomotor episodes. Perhaps with further information or localization of function in certain deeper-lying areas more of these patients might be considered as having the focal cortical clinical type of onset, since the sharp waves tend to arise from deeper-lying regions than do the spike forms.

Random Delta Activity (L 3) : Localized random delta (L 3) activity was not a good indication of focal epileptic discharge as judged from the seizure pattern, except when combined with spike or sharp wave forms.

Local Paroxysmal Rhythms (L 4): Local paroxysmal rhythms (L 4) were found mostly in patients whose attacks also suggested a focal cortical onset. Seven of the 11 patients with this type of electroencephalogram showed clinically a definite focal cortical type of onset. One showed only psychomotor episodes suggesting a discharge from the temporal lobe of indefinite laterality, with electroencephalographic

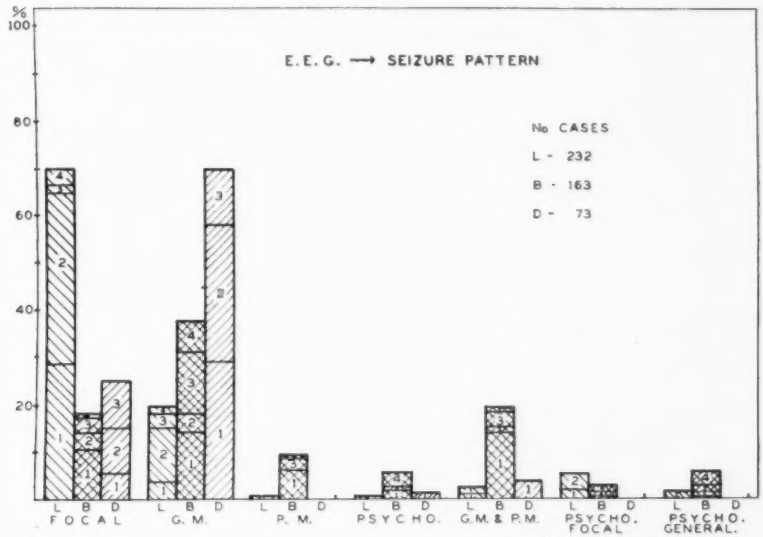


Fig. 10.—Types of seizure patterns in patients with different kinds of electroencephalograms. In this graph percentages are calculated from the electroencephalographic patterns (localized, *L*, bilaterally synchronous, *B*, and diffuse, *D*) as they are distributed among the various kinds and combinations of clinical seizures. For example, most of the patients with diffuse (*D*) electroencephalographic patterns were found to have generalized grand mal seizures (*G. M.*), with about 22 per cent having seizures judged to be of the focal cortical (*FOCAL*) type. There were none in the diffuse electrographic group who had only petit mal seizures (*P. M.*). Patients with localized abnormality in the electroencephalogram (the *L* columns) were found mostly to have focal clinical seizures (*FOCAL, FOCAL PSYCHO.*), although there was a significant percentage who seemed to have generalized attacks (*G.M.*) with no clear focal onset. Patients with bilaterally synchronous electroencephalograms (*B* column) are found distributed throughout all forms of clinical attack, with the majority showing generalized seizures, some having only major convulsions (*G.M.*), some having only petit mal attacks (*P.M.*) and others having both major and petit mal attacks (*G.M* and *P.M.*). The apparent focal cortical onset of patients in the *B* group consisted of turning of the head and eyes to one side. The small numbers in each column refer to specific forms and patterns of the electroencephalogram, as previously described.

localization in the right temporal lobe. The remaining 3 patients had generalized major seizures with no clinical evidence of focal cortical onset (fig. 11).

Etiologic Factors and Age of Onset in Cases of Localized Activity: Known etiologic factors in cases of localized electrographic disorders were those which produce discrete local lesions of the cortex, such as trauma (at or after birth), tumor, abscess or local vascular disease. The cause was unknown in about 25 per cent of the cases in this group, as compared with 50 per cent of cases in which the disorders were of the bilaterally synchronous or diffuse forms. Even in cases of localized electrographic disorder of unknown origin a local lesion was usually

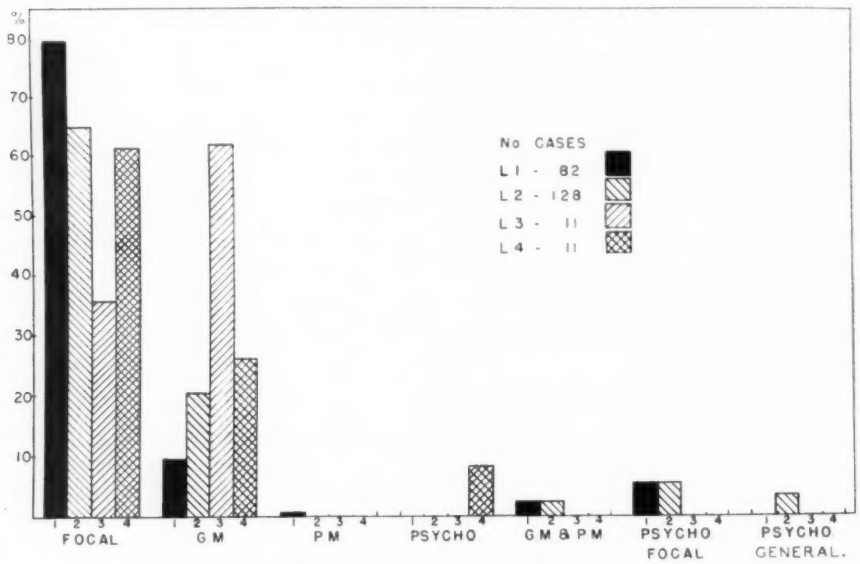


Fig. 11.—Percentage distribution of patients with localized electroencephalographic activity, showing types of clinical seizures most commonly associated with specific wave forms: (*L 1*) random spikes, (*L 2*) random sharp waves, (*L 3*) random delta waves and (*L 4*) paroxysmal rhythms.

(though not always) found either at operation or by pneumoencephalographic examination.

A local lesion, possibly operable, should therefore be assumed in all cases in which clear uncomplicated foci of spikes or sharp waves appear. The most promising results, however, are obtained with surgical therapy when the localization of the electrographic focus is corroborated by pneumoencephalographic examination and by the clinical seizure pattern.

It is of interest that in only 1 of the cases of localized electroencephalographic disorder was there a familial history of epilepsy. In

12 cases a localized disorder seemed to have developed from infectious or toxic cerebral disease. In 4 cases the clinical seizures seemed related to the menstrual cycle.

A short synopsis of a typical case follows.

M. B., a girl aged 13, had a history of attacks for one year. These attacks always began with a sensation of numbness and tingling and some pain in the finger tips of the right hand. This was followed by dizziness, and the numbness and tingling mounted up the right arm to the shoulder. She then lost consciousness; the eyes turned to the right; the right arm extended and then pronated, and there were clonic movements, usually on the right side, with drawing of the face to the right. There were frothing of the mouth and urinary incontinence. Sometimes the arm extended before consciousness was lost, but the sensation of dizziness always preceded the movement. There was weakness of the right hand and arm after attacks.

In addition, there were short attacks in which she experienced numbness and tingling and some pain in the finger tips of the right hand, which extended to the palm, without loss of consciousness. The sensation lasted about one minute and disappeared.

The major attacks occurred variably, from several daily to one a month, and the minor ones about five to six times daily.

Birth was one of prolonged labor, with postnatal cyanosis. The past personal and family histories were noncontributory.

Physical examination revealed nothing abnormal.

A pneumoencephalogram showed that the left side of the cranium was very slightly flattened as compared with the right and that the septum pellucidum was 3 mm. to the left of the midline. Portion 4 of the left lateral ventricle showed some general enlargement, chiefly upward and laterally. "The appearance suggests a focal area of atrophy in the left parietal lobe, probably close to the central fissure. The slight asymmetry of the skull suggests that this might have been present since early in life [Dr. A. E. Childe, roentgenologist to the institute]."

Electroencephalograms showed random spikes in the left parietal region with phase reversals at the standard head position P 5. From other regions of the head the records were normal.

There was a clear correspondence, therefore, between the clinical, the pneumoencephalographic and the electroencephalographic findings, all of which indicated the presence of an epileptogenic lesion in the left parietal region. A left parietal osteoplastic craniotomy was performed by Dr. Penfield, and a meningocerebral cicatrix with an area of microgyria about it was found lying just beneath the region localized by the electroencephalogram. This was removed, and the patient made an uneventful recovery.

After operation the electroencephalogram did not show any spikes and only normal alpha rhythm was obtained. The patient has remained free of attacks since operation (about eighteen months).

Patients with Bilaterally Synchronous Activity.—Bilaterally synchronous discharges were found mostly in patients (about 80 per cent) with generalized clinical seizures who showed no recognized focal cortical onset (fig. 12). This group of patients is differentiated immediately from the group with localized activity, of whom about the same per-

centage showed focal cortical clinical attacks.[22] The fact that in each group there was a discrepancy of about 20 per cent between those judged clinically to have focal attacks and those whose disturbance was localized by electroencephalogram serves to emphasize the importance of careful clinical and electrographic examination.

Bilaterally Synchronous 3 per Second Wave and Spike Activity (B 3 and 1): The 3 per second wave and spike pattern was observed in 77 cases. Major convulsive seizures were observed in 66 of these, or 86 per cent, and attacks clinically confined to petit mal (fig. 12) were noted in only 11 (14 per cent). Petit mal, either alone or combined with major attacks, was noted in 34 cases, or 44 per cent. The diagnosis

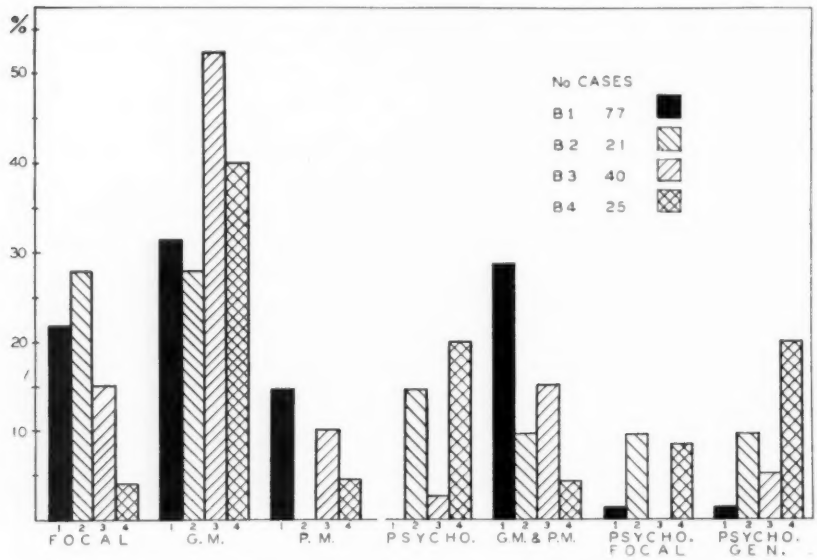


Fig. 12.—Percentage distribution of patients with bilaterally synchronous electroencephalographic activity, showing types of clinical seizures most commonly associated with specific wave forms: (*B 1*) wave and spike pattern, (*B 2*) sharp waves, (*B 3*) 3 per second waves and (*B 4*) 6 per second waves.

of petit mal epilepsy on the basis of this form of electrogram is, therefore, misleading.[23]

---

22. It is of interest to note that the patients in the group with bilaterally synchronous discharges who were thought clinically to have focal cortical seizures were so judged chiefly on the basis of onset with turning of the head and eyes to one side. This is perhaps the least reliable indication of local cortical epileptiform discharge.

23. Gibbs, Lennox and Gibbs (Arch. Neurol. & Psychiat. **43**:223-239 [Feb.] 1940) have recently found it necessary to speak of the "petit mal form of grand mal."

The important feature of the attacks in patients with bilaterally synchronous 3 per second wave and spike (B 3 and 1) electrograms is not that they are of the petit mal or the grand mal type but that their onset is generalized and usually marked by sudden loss of consciousness. Rarely is there an aura or prodrome. Associated vasomotor disturbances (flushing or blanching) are common. In the minor attacks the process goes no farther and one has what is clinically termed petit mal, "fainting spells," "absences," and the like. In the major attacks there are bilateral convulsive movements and the attacks are then called grand mal. The essential difference is one of degree rather than of kind.

The sudden loss of consciousness is a form of onset comparable to the "tingling of one hand" in patients with focal cortical seizures. In cases of focal cortical onset minor attacks may be noted as "whirling lights" when the epileptic discharge is confined to the occipital lobe. Minor attacks of the bilaterally synchronous 3 per second wave and spike (B 3 and 1) form are associated with loss of consciousness when the discharge is confined to centers (or circuits) primarily concerned with this function. All kinds of epilepsy may look alike at the height of a major seizure. It is the nature of the onset that is important. A typical case of 3 per second wave and spike (B 3 and 1) epilepsy with bilateral synchrony is described.

H. C., a girl aged 7, had a history of frequent attacks of petit mal for eight months, occasional dizziness for six months and vomiting three times in the past month.

The attacks usually occurred when she was standing or walking: Her color changed, she became pale, and then her face flushed; she stopped whatever she was doing and did not respond to questioning. She did not seem to be conscious; her eyes rolled upward, and occasionally she made a few staggering steps backward. The attack lasted from five to thirty seconds. Immediately afterward she carried on with whatever she had been doing and seemed to be perfectly normal, with no memory of the attack. The frequency and intensity of the attacks varied greatly, and they increased when she was excited.

The past personal and family histories were noncontributory. Physical examination gave essentially normal results.

Many attacks, similar to those already described, were observed during her stay in the hospital. At times, many small, irregular erythematous patches appeared over the face and neck during an attack.

A pneumoencephalogram showed slight, diffuse cerebral atrophy but otherwise nothing abnormal. The electroencephalogram showed typical bursts of wave and spike patterns, appearing frequently. These patterns were bilaterally synchronous and of highest amplitude in the frontal regions. Several typical clinical attacks, in which the blush and erythematous patches appeared and occasionally short twitches of the arms and legs occurred, were recorded electrographically, in all of which the bilaterally synchronous wave and spike pattern appeared for varying periods. The patient was sensitive to hyperventilation, and after about ten deep respirations a sudden burst of wave and spike discharges appeared.

Records taken with a basal lead [24] showed constant phase reversals of the wave and spike potentials at the basal lead. This was taken to indicate that these potentials were originating from a region lying nearer the basal lead than the surface electrodes on the scalp.

The localization of onset as determined by surface electrodes from the scalp appears bifrontal in the great majority of cases of bilaterally synchronous 3 per second wave and spike activity.[24a] A bioccipital origin is occasionally found, but no other cortical areas seem primarily involved in this form of discharge. The bilateral synchrony, together with the associated vasomotor changes, suggests a diencephalic origin for this disorder. Positive evidence in support of this hypothesis is not lacking and will be the subject of a later report.

Bilaterally Synchronous 3 per Second Waves (B 3): The 3 per second wave pattern with bilateral synchrony was observed without the spike component in 40 cases. (It was, of course, present in all of the cases classified under the 3 per second wave and spike pattern, since in all occasional slow waves without the spike were shown.) Major convulsive seizures were observed in 35 of these, or 87 per cent (fig. 12). Petit mal seizures alone were present in only 4 cases (10 per cent). Petit mal combined with other forms was observed in 10 cases (25 per cent). All patients with this form of electrogram cannot, therefore, be said to have "petit mal."

The forms of clinical seizures observed in this group are, for the most part, comparable to those already described in the cases of the wave and spike pattern. In 6 cases (15 per cent) in which there was 3 per second wave (B 3) activity, seizures were apparently of the focal cortical type and in 1 of these they were of indefinite laterality. In the others there also were some attacks the onset of which did not appear localized. Generalized bilateral seizures are the rule with onset in the form of sudden loss of consciousness. Minor attacks are of the petit mal or allied forms.

That the 3 per second wave (B 3) pattern is closely related to the wave and spike (B 3 and 1) pattern is illustrated in the case of a young girl with petit mal and generalized major seizures who had frequent

24. This is a long slender lead introduced into the inferior nasal meatus and abutting against the neighborhood of the junction of the basisphenoid and the basiocciput, modified after Grinker (Science **87**:73-74, 1938).

24a. Occasionally a wave and spike sequence at 2 to 3 per second will appear consistently from a single local cortical area before it becomes bilaterally synchronous, and many such discharges may occur from the unilateral area of onset without spread. The clinical seizures in such patients usually show some evidence of focal cortical onset. We should classify such records with the localized spike or sharp wave disorders, even though the form may appear similar to that of the bilaterally synchronous wave and spike sequence.

wave and spike discharges between clinical attacks when not receiving medication. With dilantin medication she had only the bilaterally synchronous 3 per second wave (B 3) pattern. Her mother, with only "fainting spells after running upstairs," showed prominent bilaterally synchronous 3 per second waves only after short periods of hyperventilation, and the spike component was not added even after prolonged hyperpnea (fig. 13).

Etiologic Factors and Age of Onset in Cases of Bilaterally Synchronous Wave and Spike and 3 per Second Wave Activity (B 3 and 1 and B 3): Patients with bilaterally synchronous wave and spike and 3 per second wave patterns form a fairly homogenous clinical group from the etiologic standpoint. They usually have generalized seizures beginning before or at adolescence with no apparent cause, and their disease is commonly called idiopathic. In the present study 68 per cent of the patients with this form of disorder were considered clinically to have idiopathic or cryptogenic epilepsy. A few of these patients had associated disorders of an endocrine (pituitary?) or metabolic (carbohydrate) nature. Some (6 per cent) had a strong familial history of epilepsy.

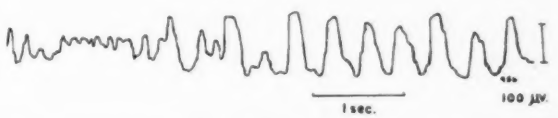


Fig. 13.—Electroencephalogram of the mother of a patient with petit mal seizures, showing 3 per second waves brought on after thirty seconds of hyperventilation. The mother had no recognized epileptic symptoms.

Familial epilepsy was not, however, confined to this electroencephalographic group.

That cases of this type may not all be relegated to the cryptogenic type of epilepsy is shown by the fact that there were 25 (21 per cent) in which the onset followed cerebral trauma (at birth or postnatal) and 11 (9 per cent) in which it followed infectious disease, (measles, whooping cough, pneumonia and syphilis). Of course, we cannot be sure that these possible etiologic agents were not incidental to a fundamental disorder or predisposition. Since no symptoms of epilepsy were previously noted, it is at least probable that this form of epilepsy may be caused by cerebral trauma or certain forms of encephalitis without constitutional predisposition. However, in 2 cases the "constitutional predisposition" was related to congenital syphilis. This question merits further study.

Bilaterally Synchronous Sharp Waves (B 2): Bilaterally synchronous sharp waves are practically all of bitemporal origin, with no definite predominance of one side or the other. They were observed in 21

cases. Patients with sharp waves localized to one temporal lobe often showed synchronous waves from the other side, a mirror focus. The cases of bilaterally synchronous sharp waves were only those in which there was good bilateral synchrony and one temporal lobe did not seem to lead more often than the other. The 6 per second wave pattern, also bitemporal, was frequently associated with bitemporal sharp waves.

Major convulsive seizures were present in 18 cases, or 86 per cent. In only 6 (28 per cent) were generalized grand mal attacks alone reported. Psychomotor episodes or episodic confusional states (ictal automatisms of Penfield) were prominent in 9 of these cases, or 43 per cent, while in 3 cases the only form of attack observed was psychomotor. In 8 (38 per cent) of the group with electrograms of this type the attacks seemed to have a unilateral focal cortical type of onset (fig. 12).

The seizures in patients with bitemporal sharp waves usually had a gradual onset, marked by various kinds of aura and complex prodromal symptoms. The most common sensory auras were vestibular, auditory, olfactory and gustatory. Vague premonitory "feelings" referred to the stomach or head (cephalic aura) and tachycardia also occurred.

The onset and minor attacks often involved disturbances in memory, thinking and behavior (automatisms—"psychomotor" episodes). The seizures of some of these patients were so bizarre that they were mistaken for hysterical attacks. It seems clear from the nature of these disturbances that the temporal lobe and subjacent structures, probably in the archipallium, are the regions primarily involved. This is in accord with the electrographic localization, which so frequently seems to be deep to the temporal lobes (e. g., the hippocampus) near the midline or to involve an area first in one temporal lobe and then in the other. A typical case is that of P. L.

P. L., a man aged 30, had attended the neurologic outpatient clinic since the age of 13. He was born at full term but was delivered with instruments. He had one convulsion at the age of 2 years but no others until he was 7. Since then attacks have occurred irregularly, varying from several daily to one a month or less.

The attacks always begin with a queer sensation in the head, which he sometimes describes as dizziness, followed by a feeling of the heart beating fast. Then he feels that the heart slows up, and there is loss of consciousness. The head and eyes turn to the left, and the mouth is twisted.

There are also spells during which the patient laughs for no apparent reason. According to his parents, although he is usually easy to get along with, there are times when he is "cranky, wilful, irritable and very sensitive."

A sister aged 22 has been having attacks since the age of 9.

The electrogram showed paroxysmal discharge of random sharp waves of large amplitude from the right and left temporal or subtemporal regions. There was perhaps a slightly greater amount from the left side, suggesting a deep-lying source. Bilaterally synchronous discharges increased during hyperventilation.

Bilaterally Synchronous 6 per Second Waves (B 4): Bilaterally synchronous 6 per second waves without the sharp wave or other forms were observed in only 25 cases. They appear at maximum amplitude from the frontal or temporal regions of the head. Some 3 cycle waves often appeared with hyperventilation.

It is the 6 cycle rhythm that is found most frequently in patients with prominent psychomotor episodes or epileptic automatisms. About half the patients with this disorder in our series presented prominent psychomotor symptoms, and 5 (20 per cent) had only psychomotor episodes, with no convulsive or petit mal seizures. Rarely are there any localizing features of the attacks, even when convulsive movements are present. It is this form of electrogram which was found most commonly in the epileptoid behavior problem children studied by Jasper, Solomon and Bradley [25] and Cutts and Jasper.[26] A typical case of this type follows.

E. S., a woman aged 20, has attended the neurologic outpatient clinic for seven years and complained of attacks of dizziness for eight years. She stated that in these attacks she "saw different visions," which lasted about a minute and were followed by a feeling of dizziness for a few seconds. She then became dazed and confused for about fifteen minutes. She often went to her mother and said that she had lost her memory, and her mother stated the belief that, though the patient carried on a reasonable conversation, memory for the immediate past was temporarily lost. There were no convulsive movements or twitching and no incontinence. In one attack, while practicing on the piano, she suddenly felt a "crazy" spell, which lasted a few seconds. She went to her mother and told her about it and then asked: "What date is it? When was Christmas? [It was actually about two weeks after Christmas.] What did I get for Christmas? Is it winter or summer?" When her mother did not answer, she became insistent. This attack was followed by headache; she lay down and went to sleep. On awakening about two hours later she had no recollection of the attack or of asking her mother these questions.

The results of physical and roentgenographic examinations of the skull were essentially normal.

For a time it was felt that these episodes might have a psychogenic basis.

The electrogram showed paroxysmal discharges of bilaterally synchronous 4 to 6 per second waves, affecting all regions of the head but highest in amplitude from the frontal areas. Hyperventilation caused an increase in the amount of this abnormal activity. Phenobarbital alone failed to control the attacks, but dilantin and phenobarbital administered together caused definite improvement.

The bilaterally synchronous 6 per second wave pattern was present in 2 cases in which marked psychotic behavior followed major convulsive attacks. One of these cases is now described.

---

25. Jasper, H. H.; Solomon, P., and Bradley, C.: Electroencephalographic Analysis of Behavior Problem Children, Am. J. Psychiat. **95**:641-658, 1938.

26. Cutts, K. K., and Jasper, H. H.: Effects of Benzedrine Sulfate and Phenobarbital on Behavior Problem Children with Abnormal Electroencephalograms, Arch. Neurol. & Psychiat. **41**:1138-1145 (June) 1939.

R. V. K., aged 28, was first admitted to the Neurological Institute at the age of 26 with a history of convulsive seizures for eight years. These seizures always began with turning of the eyes up and to the right and turning of the head to the right and then became generalized. For the last two years a period of confusion had followed the attacks. There was a history of severe injury to the head one year before the onset of attacks. A fracture was sustained which extended across the frontal bone on both sides. This was followed by an infection on the right side and the formation of a scar extending from the left temple to the hair line on the right side. There were also a scar along the lower margin of the left side of the jaw and a depression, about the size of a penny, above the right eye. Examination revealed slight weakness of the left side of the face on voluntary movement, with some diminution of strength of the left hand and a questionable plantar response on the left. The pneumoencephalogram taken during his first hospitalization showed focal atrophy, possibly accompanied by cicatrix formation involving the anterior portion of the left frontal lobe and the right temporal lobe. There was also evidence of diffuse ventricular enlargement. In September 1938 a left osteoplastic craniotomy was carried out by Dr. Penfield and a meningocerebral cicatrix was removed from the left frontal lobe. It was noted by Dr. Penfield at the time that "a second operation on the right side may have to be carried out." Two years later the patient was readmitted with a history of recurrence of attacks since about one month after operation. These attacks were preceded by yawning and a tingling sensation between the knee and the ankle in both legs. Then there was a scream, followed by loss of consciousness and clonic bilateral convulsive movements of the upper and lower extremities. These seizures occurred from three to six times during a "spell" at intervals of one or two hours; after this there would be a period of sleep for six to seven hours and a feeling of well-being and mental stability for one to three days. This was followed by a period of irrational psychotic behavior lasting for several days and then a return to well-being. During the psychotic period the patient talked continuously and incoherently, sang and wandered about aimlessly. He was occasionally violent and had to be restrained or sent to a mental disease hospital.

A series of attacks occurred during the period of observation in the hospital, and one of them, which was seen from the onset, began by turning of the eyes to the left and then to the right, followed by screaming and a generalized convulsion. In other attacks the eyes continued to be directed midline. Immediately after some of the attacks the left abdominal reflex was decreased, the left plantar response was definitely extensor and the right was of doubtful character. Two days after a series of attacks he lapsed into a "confused, religious, maniacal state," during which he was aggressive and abusive and stated that he was "the voice of the Lord," who had told him to sing. When asked where he was, he replied, "I thought I was with the Lord Jesus Christ." This state continued for a week, and he gradually returned to "normal."

Pneumoencephalographic study showed focal atrophy of the anterior portion of the left frontal lobe. There was also evidence of localized enlargement of the anterior portion of the right temporal horn, presumably indicating focal atrophy in this locality, and a moderate degree of diffuse cerebral atrophy.

Numerous electrograms were obtained. In one of them, taken after about three minutes of hyperventilation, random spikes appeared only from the right frontal pole (in the vicinity of standard head position Fp 2). The most striking finding, however, was the appearance of a continuous integrated bifrontal discharge of 4 to 5 per second waves. These waves appeared consistently in every examination.

Alpha rhythm was absent, and the synchronization of the 5 per second discharges on the two sides suggested the possibility of a subcortical common pacemaker.

Subsequently, a right osteoplastic craniotomy was performed, with the removal of a meningocerebral cicatrix from the right frontal pole. A single postoperative electroencephalogram obtained while the patient was taking dilantin and phenobarbital showed that the 5 per second rhythms were much less prominent, despite the fact that they had previously been present even with phenobarbital medication.

Etiologic Factors and Age of Onset in Cases of Bilateral Synchronous Sharp Waves and 6 per Second Waves (B 2 and B 4): Etiologic factors in disorders of this type are also largely unknown. The bilaterally synchronous sharp waves are more frequently related to definite cerebral lesions than are the other bilaterally synchronous forms. For example, in 1 case of this type there was a cyst of the septum pellucidum and in another an astrocytoma of the foramen of Monro. In 22 per cent of cases they were obtained after severe injury to the head, in 7 per cent after cerebral hemorrhage and in 11 per cent after infectious disease.

A history of familial epilepsy was not common, there being only 1 case in this series. In certain patients these bilaterally synchronous discharges may rise from the vicinity of deep-lying lesions involving certain midline structures, while the unilaterally localized discharges arise from superficial cortical lesions.

Patients with Diffuse Disorder.—In general, patients with the diffuse form of electrographic disorder have major generalized seizures, with no consistent unilateral focal onset (fig. 14). This applies particularly to diffuse multiple spikes and sharp waves (D 1 and D 2) with diffuse paroxysmal rhythms of the more rapid frequencies (D 4), rather than to the diffuse delta waves (D 3), which are not so closely related to the epileptic discharge. Minor seizures were rare in patients with diffuse rhythms. Only 3 patients had what appeared to be petit mal attacks in addition to the major convulsions, and 2 had prominent psychomotor episodes.

Diffuse Multiple Spikes (D 1): We found generalized grand mal the most common form of attack in the 29 cases in which this type of electrographic disorder appeared (fig. 14), being present in 83 per cent. In only 4 cases in this group were the seizures judged clinically to be of unilateral focal cortical onset. Since this form of activity corresponds most closely to the grand mal of the Gibbs-Lennox classification, the large proportion of generalized major seizures lends some support to their findings.

Diffuse Sharp Waves (D 2): Multiple sharp waves and slower rhythms might be considered either grand mal or psychomotor in the Gibbs-Lennox classification, more probably the latter. Most of the patients (75 per cent) with this form of electrogram had major

generalized grand mal seizures. Only 1 patient had prominent behavior automatisms (psychomotor), and 7 had seizures judged clinically to be of the focal cortical type.

Diffuse Delta Waves (D 3): Most of the patients with diffuse delta waves alone, not combined with other forms, were children with diffuse cerebral damage or dysfunction or deteriorated epileptic patients. Their seizures were usually of the generalized grand mal form, but many had also localizing features at the onset (though these were not constant).

Etiologic Factors and Age of Onset in Cases of Diffuse Disorder: In about one-half the cases in which diffuse disorders occurred the etiologic

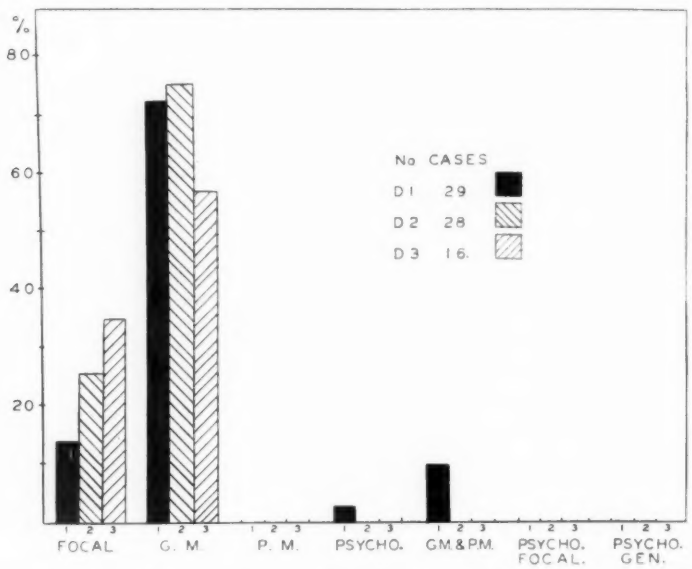


Fig. 14.—Percentage distribution of patients with diffuse electroencephalographic activity, showing types of clinical seizure most commonly associated with specific wave forms: (*D 1*) multiple spikes and rapid dysrhythmia, (*D 2*) multiple sharp waves and (*D 3*) multiple delta activity.

factors were unknown. Injury to the head (severe concussion or birth trauma) was prominent among the known causes, accounting for the condition in about 25 per cent of cases. Diffuse atrophy was a common finding in the pneumoencephalograms of patients with sharp waves and delta activity (D 2 and D 3). Infectious or toxic diseases of the brain or meninges, such as encephalitis, meningitis, syphilis, alcoholism or lead poisoning, were associated with the beginning of attacks in some patients with this electrographic pattern. In 1 case of multiple spike (D 1) activity the patient was struck by lightning. The age of onset

varied with the nature of the cause. Certain patients gave a history of familial epilepsy; for example, in one family the father showed multiple spike (D 1) activity, while the son, who clinically had a more severe condition, showed sharp wave (D 2) activity.

The clinical characteristics of patients in each electroencephalographic category are summarized in the accompanying table.

HYPERVENTILATION

It has long been known that hyperventilation may induce attacks in certain epileptic patients. Gibbs, Lennox and Gibbs [27] have made detailed studies of the effect of hyperventilation on the electroencephalogram. In our series of cases the effect of overbreathing was nearly always studied during the electrographic recording. Briefly, it was found that in nearly all patients with bilaterally synchronous 3 per second waves and spikes and 3 per second waves (B 3 and 1 and B 3) paroxysmal discharges of this form could be produced after from a few seconds to about two minutes of hyperventilation. This corroborates the findings of Gibbs, Lennox and Gibbs [27] regarding the sensitivity of these patients to hyperventilation.

It is noteworthy that many patients with bilaterally synchronous 3 per second (B 3) activity did not show 3 per second wave and spike activity (B 3 and 1) during hyperventilation, and vice versa. Patients with bilaterally synchronous 6 per second (B 4) activity were somewhat less sensitive, but the amount of this discharge was often increased and in many hyperventilation caused the appearance of 3 per second waves.

Patients with bilaterally synchronous sharp (B 2) waves were less sensitive to overbreathing than those with 6 per second (B 4) rhythms and frequently showed activity of the latter type during hyperventilation.

The other groups were much less sensitive to the effects of hyperventilation, the group with diffuse activity as a rule showing more effect than the group with localized abnormality. It should be remembered in this connection that many normal persons will show a considerable amount of delta activity, especially in frontal regions of the head, after three or more minutes of hyperventilation. At times this delta activity may be bilaterally synchronous, but usually is disorganized. However, a certain degree of caution must be exercised in interpreting the appearance of slow waves following prolonged hyperventilation (three minutes or more). Certain of the patients with localized rhythms, however, do show an increased amount of localized activity after overbreathing. The reasons for this require further elucidation.

---

27. Gibbs, E. L.; Lennox, W. G., and Gibbs, F. A.: Variations in the Carbon Dioxide Content of the Blood in Epilepsy, Arch. Neurol. & Psychiat. **43**:223-239 (Feb.) 1940.

Relation of Pattern of Clinical Attack to Electroencephalographic Abnormality

Electroencephalographic Activity		Attack Pattern		Age of Onset	Etiologic Factors
Class	Form	Major	Minor		
Localized Unilateral Cortical Activity					
L1 (17.5%)	Local random spike	Local cortical onset	Only prodrome present	Variable	Superficial local cortical lesions (trauma, tumor, abscess, local vascular)
		Pattern depends on function of cortical area of onset and path of march			
L2 (27.5%)	Local random sharp waves	Similar to that of L1	Similar to that of L1	Variable	More extensive deeper cortical lesions (trauma, tumor, abscess, local vascular)
L3 (2%)	Local random slow waves (delta)	Generalized or similar to that of L1	Variable or similar to that of L1	Variable	Local degenerative lesions of cortex (trauma, tumor, abscess, local vascular)
L4 (2%)	Local paroxysmal rhythm	Similar to that of L1	Similar to that of L1	Variable	Lesions probably more similar to those of L2
Total localized activity, 49%					
Bilaterally Synchronous Activity					
B1 (16.5%)	Bilaterally synchronous 3 per second wave and spike, usually bifrontal	Initial loss of consciousness, bilateral convulsions; some adversive movements of head and eye at onset; laterality inconstant	Disturbance or lapse of consciousness ("petit mal"); disturbance of central autonomic system (vasomotor)	Infancy to 14 yr.	Cryptogenic, endocrine, traumatic, infectious, hereditary
B2 (4.5%)	Bilaterally synchronous sharp waves, usually bitemporal	Prodrome and generalized seizures	Only prodrome	Variable	Cryptogenic, traumatic, vascular, tumor
		Disturbances in perception, memory, thinking and behavior (automatisms; "psychomotor"); auras: vestibular, gustatory, olfactory, auditory, autonomic (tachycardia, "feelings")			
B3 (9%)	Bilaterally synchronous 3 per second waves, usually bifrontal	Similar to that of B1	Similar to that of B1	Infancy to 10 yr.	Similar to that in B1
B4 (5.5%)	Bilaterally synchronous 6 per second waves, bitemporal or bifrontal	Similar to that of B2	Similar to that of B2	Variable	Cryptogenic, traumatic, infectious, endocrine, hereditary
Total bilaterally synchronous activity, 35.5%					
Diffuse Activity					
D1 (6%)	Diffuse multiple spikes	Generalized	Different forms; vague aura (visceral, etc.)	Variable	Diffuse cerebral disorder; cryptogenic, traumatic, infectious, toxic, hereditary
D2 (6%)	Diffuse sharp waves	Generalized	Similar to that of D1	Variable	Similar to that in D1, related to diffuse atrophy or metabolic disorder
D3 (3.5%)	Diffuse delta waves	Generalized	Similar to that of D1	Variable, common in infancy and with deterioration	Related to diffuse atrophy; high in intracranial pressure, general factors depressing cortical function (including injury to head)
Total diffuse activity, 15.15%					

In summary, it may be said that the increase in abnormal activity with hyperventilation is as specific a test for a true bilaterally synchronous 3 per second wave and spike and 3 per second wave disorder, as are opening and closing the eyes for true alpha rhythm.

PNEUMOENCEPHALOGRAMS

Pneumoencephalographic studies were made on a large percentage of the patients in this series. There was usually, though not always, a close correspondence between the finding of a local lesion in the roentgenogram and the presence of a localized abnormality in the electrogram (the case of M. B. is an example). Cases in which the roentgenographic and electrographic findings coincided with the clinical localization of the epileptogenic focus were those usually selected for surgical therapy. Occasionally patients with a local abnormality in the cortex as determined from the roentgenograms failed to show electrographic evidence that this was the focus of discharge of abnormal potentials, and some of these showed evidence of the disorder being bilaterally synchronous or diffuse. In others, there was localized electrographic abnormality but no roentgenologic confirmation of the presence of a local lesion. This may be due to the intrinsic differences in the methods, and further study of these differences will be carried out later.

In general, in most of the cases of diffuse activity there was evidence of diffuse generalized cerebral atrophy in pneumograms, and to a less extent this was also true of the cases of bilaterally synchronous activity. We feel that these two methods of study are mutually complementary and that the electroencephalographic method does not replace the older, roentgenographic method. In fact, the tendency has been for these two methods to stimulate interest in studying each case more extensively as an individual problem.

COMMENT

The most significant result of the analysis of electroencephalographic and clinical observations on epileptic patients presented here, in our opinion, is the establishment of a specific form of electrogram for patients with seizures of focal cortical onset. A single, well restricted focus of random spikes or sharp waves, with normal activity from all other regions of the head, usually leads to the site of onset of an epileptic seizure as judged by the clinical seizure pattern, and in many cases this has been verified by operative exploration and electrical stimulation. Without the necessity of observing a clinical attack, the electrogram therefore provides a reliable guide to further study of the possibility of successful

surgical therapy.[28] The first step in classification, therefore, is to differentiate between those patients who have a superficial cortical focus and those with deep-lying foci or generalized abnormality.

Patients judged to have focal cortical epilepsy have widely different forms of seizure. In all, the form of clinical symptoms depends on the function of the cortical area primarily involved. The form of electrographic discharge is the same in all cases, but the localization differs. All seizures may look nearly alike at the height of a major attack after it has become generalized. Differences are due to localization of onset and path of march. If this principle applies to seizures arising from superficial cortical areas, it may apply also to seizures arising from other parts of the brain.

The judgment of focal cortical onset is based almost entirely on knowledge of functional localization in exposed cortical areas. Likewise, localized cortical discharge revealed by the electroencephalogram must also refer chiefly to cortical areas subjacent to the calvarium. Patients who fail to show a focal cortical onset in the seizure pattern or a localized discharge in the electroencephalogram may still have seizures with focal onset. Discharges arising from deeper-lying cortical areas, e. g., the paraolfactory areas of the frontal lobes, the island of Reil or the hippocampal gyrus, might well appear bilaterally synchronous in the electrogram when projected to the cortex subjacent to the calvarium.

If the focal disturbance begins in subcortical structures, such as the thalamus, the hypothalamus or the basal ganglia, large areas of the cortex of both hemispheres may be involved as a result of impulses radiating from central projection nuclei. In these cases, as in those of superficial cortical onset, the form of the seizure depends on the function of the local area of onset and the path of the march. Failure to recognize the precise focus of onset is due to lack of knowledge regarding the function of these deeper-lying structures and of their relation to general cortical function.

It is the bilaterally synchronous discharges that seem most probably due to a deep-lying central focal pacemaker. The best example is the wave and spike and the 3 per second wave forms with bifrontally synchronous onset.

In case of the diffuse disorders there is no electrographic or clinical evidence for a single focal onset for all attacks. There appear to be multpile foci, with the major discharge shifting from one point to another at different times. Disorders of this kind seem truly nonfocal, while bilaterally synchronous discharges may arise from deep-lying foci.

28. This does not mean that in all cases in which random spike or sharp wave foci appear operation should be performed on the basis of electroencephalographic evidence alone. Operative exploration was carried out in only about 30 per cent of these cases in this study.

The specific forms of the electrogram do not necessarily imply essentially different abnormalities in the biochemical reactions of the brain, as suggested by the studies of Gibbs, Lennox and Gibbs.[27] They may be similar kinds of disorder with different localizations. Both the form of clinical seizure and the electrogram may be related to the specific organization of neuronal discharge, the circuits involved and their relation to the recording electrodes. Superficial disturbances in different cortical areas may appear of the same form because they are recorded directly at their source. Conducted disturbances from deep-lying projection nuclei may appear of different form when recorded indirectly at the cortex.

Biochemical factors cannot be overlooked, but the most reasonable working hypothesis to be derived from the data available is that differences in the form of clinical seizures, as well as in the form of electrograms, are due to localization of neuronal cells and circuits rather than to fundamental biochemical differences in the neurons. We do not mean to imply that biochemical agents do not cause epilepsy. Epilepsy is a symptom of excessive discharge in nerve cells, whatever may be the cause. The form of seizure is related to the particular neurons involved, rather than to the etiologic agent. This applies to widespread discharge of many neurons or to focal discharge of a few.

Characteristic electroencephalographic patterns have been found in carefully selected patients who had only minor attacks of the type described as petit mal or psychomotor. The form of these patterns is the same as that originally described by Gibbs and Lennox and called by these names. Why is it, then, that these same electrographic patterns were so often found in clinically unselected patients subject to major convulsive seizures and who did not show prominent petit mal or psychomotor symptoms? It would seem that the terms "petit mal" and "psychomotor" are not adequate descriptions of the complete disorder in these cases.

If one considers the terms "petit mal" and "psychomotor" to refer to the clinical form of onset only, and classification is based on the symptomatic form of onset, there may be some justification for the use of these terms. However, since "petit mal" has long been accepted as meaning only a minor attack and "psychomotor" as meaning only certain forms of epileptic automatisms, we prefer not to use these clinical terms to describe electroencephalographic patterns which are found in so many patients whose attacks are not commonly placed in these categories. Electrographic terminology such as used in this study avoids this dilemma.

With regard to the term "grand mal," patients selected clinically as having only major generalized convulsions did not have a characteristic type of electroencephalogram. However, electrographic selection of

patients with diffuse multiple spikes and rapid rhythms, the "grand mal pattern" of Gibbs and Lennox, did give us a group of patients who had mostly generalized major convulsions. With regard to the clinical and electrographic relations, our data seem to corroborate those of Gibbs and Lennox concerning cases of pure petit mal and psychomotor episodes by clinical selection and of grand mal by electrographic selection.

In the case of petit mal and psychomotor states one is dealing with minor attacks and in that of grand mal with major seizures. Minor attacks in patients with diffuse multiple spikes are usually evident only in the electrogram. They are clinically of a form not usually recognized as attacks (anxiety, vague feelings of gastric uneasiness, nausea, faintness and the like). Grand mal attacks, as usually understood clinically, may occur in patients with any form of electroencephalogram or type of onset, so that it becomes a meaningless term either for electroencephalographic or for clinical classification. The terms petit mal and psychomotor (we prefer "automatisms") refer to types of onset, as judged by the results of this study, and are therefore useful in the clinical differentiation of epileptic patients. They still refer to clinical symptoms and should not be used to describe phenomena of an entirely different order: disturbances in the electrical activity of the brain.

SUMMARY AND CONCLUSIONS

Definite abnormalities of a paroxysmal character were observed in the electroencephalograms of 468 of a total of 496 epileptic patients examined, or 95 per cent. A total of 936 records, taken mostly between clinical seizures, were analyzed and the various forms of abnormality classified without reference to other clinical data. The pattern of clinical attack was then related to the electroencephalographic findings, as were also possible etiologic agents. The principal results are summarized in tabular form.

1. Sudden outbursts of high voltage waves, called paroxysmal hypersynchrony, were the distinguishing feature of electroencephalograms obtained from epileptic patients. This excessive cortical discharge may occur without abnormal frequencies (dysrhythmia).

2. Localization was found to be the most satisfactory basis for classification of electroencephalographic records. The three principal kinds were (*a*) localized unilateral cortical, (*b*) bilaterally synchronous from homologous areas and (*c*) diffuse.

3. Wave forms and patterns were important for the detailed analysis of each case. They were divided into random waves and paroxysmal rhythms. Three types of random waves were spikes, sharp waves and delta waves. The six forms of paroxysmal rhythm were 3 per second

waves and spikes, 3 per second waves, 6 per second waves, 10 per second waves, 14 per second waves and 25 per second waves.

4. Abnormality localized to a discrete area of one hemisphere was found in about one-half the cases studied. The principal localized forms were random spikes, random sharp waves, random delta waves and paroxysmal rhythms. The random spike was the best indication of superficial local cortical epileptic discharge. Seizures with focal cortical onset and gradual march were most common in patients with this pattern, the specific type of onset being related to the function of the cortical area primarily involved.

5. Bilaterally synchronous abnormality, observed in 35 per cent of cases, appeared chiefly bifrontal or bitemporal and occasionally bioccipital. The principal forms were the 3 per second wave and spike pattern, sharp waves, 3 per second waves and 6 per second waves. The 3 per second wave and spike rhythm and the 3 per second waves were usually bifrontal and were often present in the same patient, with minor attacks usually of the petit mal form and major attacks which became generalized, with initial loss of consciousness at the onset. Sharp waves usually appeared as bitemporal and were present in patients with onset of major seizures and minor attacks referable to structures lying within or deep to the temporal lobes. Many had visceral auras with complex disturbances of thinking or behavior (automatisms; psychomotor attacks). Six per second waves appeared either as bifrontal (often associated with 3 per second waves) or as bitemporal, when associated with the sharp wave forms. Visceral auras and epileptic automatisms were often prominent.

6. Diffuse abnormality, without bilateral synchrony, was found in about 15 per cent of the cases. Three principal forms were diffuse multiple spikes, diffuse multiple sharp waves and diffuse multiple delta activity. Patients with diffuse multiple spikes and diffuse multiple sharp waves most commonly had major generalized seizures with no consistent focal cortical onset.

7. The pattern of clinical seizure shows a close relationship to the form of the electroencephalogram, particularly with regard to localization. The localization of specific groups of neurons the excessive discharge of which marks the onset of an epileptic seizure and existing relations between these primary foci and the rest of the brain may determine both the form of the electroencephalogram and the pattern of clinical seizure, independent of the nature of the etiologic factor in each case.

INVOLUTIONAL MELANCHOLIA

A REVIEW WITH ADDITIONAL CASES

AUGUST A. WERNER, M.D.
Assistant Professor of Medicine, St. Louis University School of Medicine
ST. LOUIS
AND
EMMETT F. HOCTOR, M.D.
AND
C. C. AULT, M.D.
FARMINGTON, MO.

Probably the first biologic urges of primitive man were what are now called instincts. Closely associated with instincts are the emotions. The emotions represent psychic responses to internal and especially to external stimuli. These responses are mediated through the central and autonomic nervous systems and the hormones of the endocrine glands.

It is known that dysfunction of these ductless glands, by over or under supply of their hormones, can so disturb persons emotionally that they manifest psychoses. Thus psychoses occur in cases of hyperthyroidism, hypothyroidism and pituitary-gonad imbalance. The hormonal conflicts of pregnancy and the necessary postpartum readjustments may cause profound disturbances of the personality. Tremendous emotional upsets result also from fright, fear and anger. Under these conditions a large amount of epinephrine is released by the adrenal glands. This epinephrine acts on the neuromuscular end plates of the sympathetic division of the autonomic nervous system and prepares the person and releases energy for defense. The subject becomes nervous and excited and certainly does not conduct himself as an undisturbed person during this stimulation.

Alvarez [1] appropriately stated:

> The physician's hardest job often is to convince a patient with functional troubles that all his symptoms are due to misbehavior of nerves connected with a tired brain. . . . Most of the symptoms of these persons suggest an instability of the involuntary nervous system which causes it to play disconcerting tricks on a normal heart, blood vessels, digestive tract, kidneys and skin. The symptoms suggest storms running out along the autonomic nerves.

From the Department of Internal Medicine, St. Louis University School of Medicine (Dr. Werner) and Missouri State Hospital No. 4 (Dr. Hoctor and Dr. Ault).

1. Alvarez, W. C.: New Light on the Mechanisms by Which Nervousness Causes Discomfort, J. A. M. A. **115**:1010 (Sept. 21) 1940.

In the normal person there is a sort of thermostat situated in the hypothalamic nuclei at the base of the brain which controls the involuntary nerves and the glands of internal secretion so perfectly that the organs of the body function silently: so silently that the owner is unconscious of them. Normally this "thermostatic center" is kept in control by the cerebral cortex. When this control is removed in any way, the center works erratically, and storms go out to cause upsets in the functions of many of the organs of the body.

To this we might add that while in some of its functions the cerebral cortex exercises a conscious control over the emotional reactions, its stabilizing influence can be disorganized by failure of proper function of such an important part of the autonomic control as is inherent in the endocrine glands.

At the present time hardly any one questions that there is an endocrine-autonomic syndrome for castration, ovarian hypofunction and the menopause.[2] This syndrome has been adequately described and published and has been utilized as a basis for diagnosis of these conditions.

After much observation over a period of years of large numbers of patients having mild to extreme menopausal symptoms, Werner and associates[3] concluded that so-called involutional melancholia is only the severest manifestation of the disturbances at this period in life. Knowing the efficacy of estrogen in relieving the distress of patients exhibiting the castrate-menopausal syndrome, they decided to treat with it a group of carefully controlled patients having involutional melancholia. The results obtained in this series of experiments were gratifying and have been published.

However, as is beneficial to science, all clinicians and investigators do not fully agree that the aforementioned deductions are correct. Robinson[4] stated, "As far as is known, there is no mental disease that is due exclusively to glandular afunction or dysfunction. Every patient has a strong psychopathologic content which must be considered."

---

2. Werner, A. A.: Symptoms Accompanying Ovarian Hypofunction, J. Missouri M. A. **28**:363 (Aug.) 1931; Syndrome Accompanying Deficiency or Absence of the Ovarian Follicular Hormone: Study of 197 Cases, Endocrinology **19**:695 (Nov.-Dec.) 1935; Endocrinology: Clinical Application and Treatment, Philadelphia, Lea & Febiger, 1937.

3. (*a*) Werner, A. A.; Johns, G. A.; Hoctor, E. F.; Ault, C. C.; Kohler, L., and Weis, M. W.: Involutional Melancholia: Probable Etiology and Treatment, J. A. M. A. **103**:13 (July 7) 1933. (*b*) Werner, A. A.; Kohler, L. H.; Ault, C. C., and Hoctor, E. F.: Involutional Melancholia: Probable Etiology and Treatment, Arch. Neurol. & Psychiat. **35**:1076 (May) 1936. (*c*) Ault, C. C.; Hoctor, E. F., and Werner, A. A.: Theelin Therapy in the Psychoses, J. A. M. A. **109**:1786 (Nov. 27) 1937.

4. Robinson, G. W.: Treatment of Depression and Melancholia, J. Missouri M. A. **37**:65 (Feb.) 1940.

This is equivalent to stating that if the patient has not previously been psychopathic, then he or she cannot become psychotic because of endocrine disturbance. We have seen severe disturbances develop at this period in great numbers of patients who had been very stable throughout life. It is granted that a person having a very unstable endocrine-autonomic nervous system may have more severe mental difficulty in the period of adjustment, but that such instability is a prerequisite for psychosis is not granted.

Robinson stated further, "Results in our own series of twenty patients with involutional melancholia (up to 1938) treated with theelin were sixteen with little or no change, two noticeably improved and two apparently well. The last two were rather mild in their manifestations." The amount of estrone (theelin) used was 6,000 units per week; there is no information as to the length of treatment. While we formerly recommended the use of this small amount, we have found that larger doses are more effective in menopausal psychoses. We have since given as much as 10,000 to 20,000 international units every other day until the patient improved, and then the quantity has been reduced to maintenance level.

Ripley, Shorr and Papanicolaou [5] reported on the treatment of 20 patients of the menopausal and the postmenopausal age group suffering from depression as follows:

> The patients in this investigation fell into three diagnostic groups: (1) seven cases of involutional depression; (2) six cases of depression of the manic-depressive type; and (3) seven cases of depressive illnesses of a more reactive nature. In some patients of this last group inherited tendencies to depression were present as well as psychoneurotic factors. The ages ranged from 39 to 58 years.

They concluded:

> In the group of menopausal and post-menopausal depressions studied the beneficial effect of estrogenic hormone was confined to the relief of vasomotor symptoms with associated improvement in feelings of well-being. There was no evidence that the depressive illness as such was influenced specifically or its course shortened.

The objection to the report of Ripley and co-workers is that while 20 cases of depression occurring during the menopause are reported, only 7 of these are cases of involutional depression. The other 13 cases are instances of types of depressive psychosis, for which there is no proof of an endocrine cause. We recommended treatment with estrogen only for true involutional melancholia.

---

5. Ripley, H. S.; Shorr, E., and Papanicolaou, G. N.: The Effect of Treatment in the Menopause with Estrogenic Hormone, Am. J. Psychiat. **96**:905 (Jan.) 1940.

Schube, McManamy, Trapp and Houser [6] stated that they had 30 patients with involutional melancholia, 20 women and 10 men. Of these they chose 6 women and 4 men, who they felt would not recover, to be treated.

It might have been better had they classified all their women patients according to the chances of recovery—good, fair and poor. They could then have divided the patients into 2 groups, one group to be given estrone and the other, physiologic solution of sodium chloride for its psychic effect.

Why include in the group of 10 to be given estrone 4 men? Estrone is a female principle and when injected into a woman should benefit her if it had been needed. We know, on the other hand, the effect of excessive androgen on a woman, e. g., masculinization. Could not, in an analogous manner, the estrone given to these men have disturbed their endocrine balance and caused them to become worse? The 30 per cent of the 10 patients, who were made worse by treament with estrone, patients 4, 6 and 8, were men, as one would expect. Androgen was available; it would have been correct to administer it to these men. The results observed in these men do not constitute evidence for the inefficacy of estrogen and must be eliminated from consideration. In the group used as a control, which received no treatment, 20 per cent of the patients recovered. According to statistics, this is the normal rate of recovery for untreated involutional melancholia.

Their patients were given 300 rat units of estrone in oil three times a week for ten weeks.[7] These patients were not treated for a sufficiently long time. We, after consulting our experience in the treatment of castrates and patients during menopause, decided on a period of six months as a fair trial for treatment. We found that some patients require longer than six months and some less. The duration of treatment depends on the response of the individual patient, and no arbitrary time can be established for treatment. This holds good for the treatment of any illness.

One of their patients had regular monthly periods established after four weeks of treatment with estrone but without alteration of her mental condition. This was to be expected. Uterine bleeding during the climacteric is not proof that the woman has normal endocrine function. It is not unusual for women to have uterine bleeding during this period and at the same time to have the symptoms characteristic of the menopause. In fact, cessation of menstruation is not the climac-

6. Schube, P. G.; McManamy, M. C.; Trapp, C. E., and Houser, G. F.: Involutional Melancholia: Treatment with Theelin, Arch. Neurol. & Psychiat. **38**:505 (Sept.) 1937.

7. This amount, which we recommended after our first experiment, is now known to be altogether inadequate in many cases of involutional melancholia.

teric; it is only visible evidence that the woman is having glandular imbalance. The climacteric is the result of this glandular dysfunction, and its systoms will be present until the endocrine adjustment characteristic of the postmenopausal period is established.

EVIDENCE FOR HORMONAL CONCEPT OF INVOLUTIONAL MELANCHOLIA

Since the original experimental investigations of the effect of estrone treatment on involutional melancholia were reported by Werner and associates [3] in 1933, additional confirmatory reports have been published by other and capable investigators.

It is reassuring to have the consonant opinion of such psychiatric authorities as Strecker and Palmer,[8] who stated:

> Involutional melancholia is a psychosis occurring during the physiologic epoch common to men and women known as the involutional period, "change of life," or climacteric. It is especially important in the present day that the physician recognize the earliest manifestations in the inception of this illness, since during the past five years, new and highly specific therapeutic weapons have been provided in the form of glandular extracts. It is possible by the prompt and judicious use of endocrine products to reduce the physiologic stresses of this period and to turn the tide toward mental equilibrium. . . . Knowledge of the physiological and endocrine stresses which both male and female persons suffer during the involutional period has been tremendously advanced in the past five years. It is definitely known and generally accepted that many of the symptoms, formerly regarded as psychogenic in origin, actually have their basis in glandular maladjustments incident to this epoch.

Strecker and Palmer then cited a case (page 109) which, they stated, "will serve to illustrate the highly specific effects of endocrine therapy." The patient, a woman aged 48 years, was treated with injections of estrone with satisfactory readjustment.

Little and Cameron [9] reported that 11 patients with mental disturbance occurring in connection with the menopause responded without exception to estrone therapy. They stated: "From the results of this investigation it may be seen that where anxiety symptoms seem to arise from the abnormal action of the endocrine glands governing sex activity, the use of theelin appears to be almost specific." On psychoses not associated with the menopause "the effects were doubtful."

Additional evidence was submitted by Mazer and Israel,[10] who treated a group of 33 patients presenting severe climacteric symptoms. Three

8. Strecker, E. W., and Palmer, H. D.: The Recognition and Management of the Beginning of Mental Disease, in Psychiatry for Practitioners, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1940, vol. 7, p. 101.

9. Little, G. A., and Cameron, D. E.: Effects of Theelin on Anxiety, Canad. M. A. J. **37**:144 (Aug.) 1937.

10. Mazer, C., and Israel, S. L.: Symptoms and Treatment of Menopause, M. Clin. North America **19**:205 (July) 1935.

had attempted suicide, and 3 others were obsessed with desire for self destruction. Not 1 of the 33 patients, despite the severity of their symptoms, failed to respond to estrogenic therapy.

Tarumianz,[11] in discussing "Psychiatric Implications of Endocrine Disturbances," stated that in many cases of involutional melancholia in which treatment was given at the Delaware State Hospital estrone was used with success.

Dynes[12] treated 7 patients having involutional melancholia with estrogen. He stated:

> Except in two cases, clinical improvement was definitely correlated with demonstrated effectiveness of the estrogen [by vaginal smears]. The lessening and abolition of the acute agitation and tension were noted to occur from two to five weeks after the beginning of estrogenic therapy. The failure of this type of therapy [in 2 cases] was attributed to irreversible physiologic changes.

Suckle[13] reported successful treatment of involutional melancholia with estrogen in 2 cases.

The Annual Report from the New York Hospital, Westchester Division, stated that 50 per cent of the patients given estrogenic therapy for involutional melancholia responded well.

Since the original experiments were reported in 1933, we[3c] published in 1937 the results of estrone treatment of involutional melancholia in 14 additional cases. In this second group, made up of 14 women, 11 recovered, became socially adjusted in a few months and were allowed to return home. Of the other 3 patients, 1 had been treated only two weeks and showed a slight improvement; 2 had been treated four weeks and showed moderate and slight improvement respectively. All 3 have since become adjusted.

Since the publication of our last article, in November 1937,[3] a third group, made up of 13 women averaging 43.6 years of age, has been treated at Missouri State Hospital No. 4, Farmington, Mo.[14] Each of the 13 patients became socially adjusted and was paroled. The average duration of the psychosis before admission to the hospital was fifty-three and one-half days; the average time of treatment before parole was three months. Among these 13 women was a castrated woman, aged 32 years, who became adjusted within two months. The symptoms

---

11. Tarumianz, M. D.: Psychiatric Implications of Endocrine Disturbances, Delaware State M. J. **8**:93 (June) 1936.

12. Dynes, J. B.: Estrogenic Therapy of Involutional Melancholia, Arch. Neurol. & Psychiat. **42**:248 (Aug.) 1939.

13. Suckle, J. E.: Treatment of Involutional Melancholia by Estrogen, J. A. M. A. **109**:203 (July 17) 1937; personal communication to the authors.

14. Ault, C. C.; Hoctor, E. F., and Werner, A. A.: Involutional Melancholia: Additional Report, Am. J. Psychiat. **97**:3 (Nov.) 1940.

of involutional psychosis in this castrated woman did not differ from the symptoms exhibited by patients with true involutional melancholia; this fact tends to confirm the endocrine basis for this condition.

Table 1 gives data on 9 additional patients with involutional melancholia treated by one of us (A. A. W.) with estrone. Table 2 summarizes the results of our treatment of involutional melancholia with estrogen in 68 patients since 1934.

It will be noted that in the original experiment, in which we had 32 patients with true uncomplicated involutional melancholia, 8 patients

TABLE 1.—*Data on Nine Patients Treated with Estrone*

Name	Age	Duration of Psychosis Before Admission	Treatment Before Adjustment
C. P.	48	8 months	5 months
H. S.	57	2 years	2 months
M. T.	49	1 year	3 weeks
B. McE.	48	8 years	2 months
R. D.	48	6 months	1 month
H. H.	30	3 months	5 months
A. M.	40	3 months	2 months
D. P.	44	3½ months	6 months
R. S.	39	5 months	6 weeks
Average			2.8 months

TABLE 2.—*Results of Treatment of Sixty-Eight Patients with Involutional Melancholia by Administration of Estrone*

Experiment	Number of Patients	Average Age of Patients	Average Age at Onset of Symptoms	Patients Socially Adjusted	Patients Failing to Adjust
Original	32	50.3	47.0	24	8
Second	14	44.3	44.3	14	0
Third	13	43.6	43.6	13	0
Private (Werner)	9	44.8	44.8	9	0
Total	68				
Average		45.7	44.9		
Percentage				88.2+%	11.8%

did not become socially adjusted. It will also be noted that in the original group the average age was 6.1 years older than that of the other 3 groups. Some of these women had been in institutions for an extended period of years; in one instance the woman had been in the sanatorium for eleven and four-tenths years. It is recognized that when patients have been psychotic for some time, there is a tendency to mental deterioration which may be irreversible. The last 3 groups of patients were subjected to treatment soon after the onset of the psychoses; as a result, the response to treatment was quicker and more definite.

Treatment of the original group of patients was of necessity experimental; we have since found that the doses used in the treatment of this group were inadequate in some instances, especially for patients who had been long ill and severely disturbed mentally.

More recently we have noted that it is more effective to administer 10,000 to 20,000 international units of estrone every other day than 2,000 international units every other day. The larger doses are to be given until the patient shows marked improvement and then may be decreased to 2,000 international units every other day. When the patient is paroled, treatment should be continued for a few months. Then the relatives should be warned that if there is evidence of recurrence, treatment should be reinstituted at once.

DURATION OF THE CLIMACTERIC

It is important to stress that the climacteric varies in time of occurrence and in duration with each person just as the menacme does. Some women enter the climacteric at 38 and others at 50 years of age. Frequently a woman menstruates until the age of 56. In some women the symptoms of the climacteric period may be fleeting or hardly noticeable; in others, the syndrome may last from three months to five or six years and even longer. Some women have claimed they had no appreciable disturbance at the time they ceased to menstruate and then five or ten years later, at ages from 50 to 60 years, experienced the typical menopausal syndrome, which responded to treatment.

If a woman whose climacteric lasts only three to six months (time at which endocrine equilibrium occurs) should experience involutional melancholia and be properly treated with estrone for six months, with recovery, one can expect that there will be no relapse. If, however, a woman whose climacteric disturbance continues four to five years should acquire involutional melancholia, she will need prolonged and intermittent treatment. She should be studied, and if there is evidence of recurrence she should be treated at once before a severe relapse occurs.

COMMENT

The pathogenic mechanism of the climacteric symptom complex is not limited to insufficiency of the ovaries but is the result as well of a complex endocrine crisis, which varies in different persons. In this crisis the predominating feature is gonadal insufficiency, but other glandular disturbances subsequently occur and are an essential part of the complex. Because of the major importance of the gonads in the endocrine system during active sexual life, insufficiency or cessation of

function frequently causes imbalance in other interrelated glands, such as the anterior lobe of the pituitary, at times the posterior lobe, the thyroid and the adrenals.

With this disturbance of function in the ovaries and other interrelated glands, there is a secondary disturbance of the delicate equilibrium between the two divisions of the autonomic nervous system with the consequent production of the subjective symptoms we have described. In other words, most of these symptoms are the result of an instability of the autonomic nervous system secondary to glandular imbalance.

In some women and men this endocrine-autonomic imbalance is so severe that they manifest an exaggerated form of the climacteric syndrome and become psychotic.

SUMMARY AND CONCLUSIONS

1. Treatment of 68 patients having involutional melancholia with estrone led to social readjustment in 88.2 per cent of the patients.

2. As a result of our experience over a period of years in treating patients having involutional melancholia and from knowledge of the experience of others, we are impelled to believe that our original observation is correct, namely, that involutional melancholia is an exaggerated form of the climacteric syndrome.

3. From our own experience and that of others, we are convinced that estrogenic substances are very efficacious in relieving involutional melancholia and in assisting the patients to social readjustment.

4. Larger doses of estrone than we first recommended should be administered. Instead of 1,000 or 2,000 international units every other day, doses of 10,000 to 20,000 units should be used until the patient shows improvement.

THE PARANOID SYNDROME

CHARLES W. MILLER JR., M.D.
MEDICAL LAKE, WASH.

A review of the psychiatric literature dealing with paranoia and the paranoid disorders [1] reveals the fact that most of the writings on the subject, with a few notable exceptions, may be divided into two main groups. The earlier writers used a descriptive approach and concerned themselves chiefly with distinctions between supposed nosologic entities, while later authors, who preferred an interpretative method, often reached their conclusions after an intensive study of only a few cases. Rarely was attention given to paranoid reactions occurring outside the major functional paranoid psychoses, save for the purpose of drawing fine diagnostic distinctions. With the tendency, on the one hand, to classify and reclassify every deviation of symptom patterns from an arbitrary norm and the tendency, on the other, to make each case the basis not only for a new theory of etiology, but sometimes for a cosmogony as well, it is not surprising that some aspects of the knowledge of the paranoid disorders have often appeared to be of dubious value.

Accordingly, it was thought profitable to study a large group of cases in which paranoid symptoms were exhibited, by every available approach and from the point of view that the reactions encountered are not necessarily to be considered as circumscribed diseases, but may rather be regarded as symptom complexes, which are often merely exaggerations of an almost universal mode of reaction to various life situations. Although it was necessary to eliminate from the study some patients concerning whom it was impossible to obtain reasonably accurate information, or who were so inaccessible as to render futile any attempt at an interpretative approach, no other effort was made to select the material. Since it was suspected that the paranoid reactions which appear in full-blown form cannot be considered entirely unrelated to those paranoid trends which may break forth under the impact of an organic illness, or which occasionally modify the form of an illness which is not predominantly paranoid in character, the cases were chosen without undue concern for the diagnosis attached, and the mere pres-

From the Eastern State Hospital.

1. See the historical survey in the bibliography in Muncie, W.: Psychobiology and Psychiatry, St. Louis, C. V. Mosby Company, 1939, pp. 660-679.

ence of paranoid symptoms, whether prominent or incidental, chronic or transient, was sufficient for inclusion in the group. As a result, in the series of 400 cases studied, there appeared 152 instances of paranoid schizophrenia, 40 of other types of schizophrenia, 63 of senile and arteriosclerotic psychoses, 38 of paranoid condition and paranoia, 36 of manic-depressive psychosis, 21 of involutional psychosis and 18 of syphilis of the central nervous system, as well as smaller numbers of cases of psychoses associated with somatic disease, mental deficiency

Statistical Summary of Some Findings in the Study

	Paranoid Schizophrenia	Other Schizophrenia	Mental Deficiency	Involutional Psychoses	Alcoholic Psychoses	Senile and Arteriosclerotic	Manic-Depressive	Paranoid State	Syphilis	Somatic Disease	Epilepsy	Trauma	Unclassified	Total Number
Sexual and marital adjustment														
Married	79	12	6	20	3	53	34	34	10	8	2	3	4	268
Unmarried	73	28	1	1	2	10	2	4	8	2	1	0	0	132
Divorced	30	2	4	6	2	22	4	18	0	6	0	2	2	98
Incompatibility or separation	12	4	0	0	1	6	6	2	4	2	2	0	2	41
Happy marriage	32	4	0	14	0	23	16	10	4	0	0	1	0	104
Promiscuity	14	0	6	0	2	0	2	0	9	2	0	0	0	35
Abnormal shyness	22	18	0	0	0	0	0	0	0	0	0	0	0	40
Misogamy	15	0	0	1	1	6	0	3	0	0	0	0	0	26
Methods of dealing with difficulties *														
Violence	27	4	0	0	0	11	4	6	4	0	0	0	0	56
Resort to physician	6	2	0	3	0	2	0	0	0	1	0	0	2	16
Resort to clergyman	1	1	0	0	0	1	0	0	0	0	0	0	0	3
Resort to police	24	3	0	2	1	7	6	2	2	1	0	2	2	52
Flight	36	12	3	4	4	10	8	9	2	2	0	0	2	92
Admission to hospital	6	0	0	2	0	0	0	0	0	2	0	0	0	10
Alcohol	2	0	0	0	0	0	3	0	0	0	0	0	0	5
Purposeless behavior	21	10	2	8	0	14	7	6	2	4	3	0	0	77
Resort to relatives	27	0	2	2	0	1	4	0	2	0	0	0	0	38
Legal action	0	0	0	0	0	0	4	7	0	0	0	0	0	11
Threats	16	8	0	0	0	17	2	10	6	0	0	1	0	60
Total no. of patients	152	40	7	21	5	63	36	38	18	10	3	3	4	400

* A few patients were listed under several headings in this section.

and epilepsy and psychoses due to alcohol and trauma. There were also a few cases in which the illness resisted classification.

Many of the findings in this study did not easily lend themselves to a brief report, and, because of the requirements of space, it was necessary to ignore some aspects of the problem in order to give sufficient attention to the detailing of the more interesting facts, although even these had to be presented with brevity. If resort was occasionally had to generalities delivered in the guise of statistics, it was only with full realization of the inadequacy with which figures can describe the intensely individual experiments which make up the pattern of the psychoses.

Attention was first centered on the positive findings, and of these one of the most outstanding was the apparent relationship and similarity of the paranoid reactions occurring in the various diagnostic groups. Although there were obvious differences in the prominence and permanence of the symptom complexes as they appeared in various disorders, it did not seem possible to establish any sharp demarcation between them. Certain symptomatic distinctions [2] could be made, it is true, but even these were not sufficiently marked to justify the consideration of the reaction of a senile paranoid patient, for example, as something apart from that of a true paranoia. Rather, it seemed to be the degree to which certain aspects of the personality were present and the stresses to which the person was subjected which determined whether he was more or less normal, whether he was merely peculiar, whether he early took refuge in a functional psychosis with paranoid coloring or whether symptoms appeared only after the occurrence of an organic illness in old age. The degree of affectivity present, consideration of which is accorded an important place in many tables of differential diagnosis, seemed to belong more properly to the illness with which the paranoid complex was associated than to the paranoid symptoms themselves. Hence it was felt justifiable to study and report on the patients as a group, noting the similarities, as well as the differences, which became apparent during the investigation of various aspects of their illnesses.

In the study of the group as a whole, one of the most remarkable features was the frequency with which inadequate or unsatisfactory sexual and marital adjustments [3] were observed. Of the 268 married persons in the group, 98 obtained a total of 122 divorces, while an additional 41 contracted marriages which were so incompatible that they ended in separation or serious consideration of divorce. Prominent traits of jealousy and suspicion marred the marriages of still others, so that, even though measured by moderate standards, it was possible to discover only 104 persons whose marriages could be described as reasonably stable and happy. Of those not married, 35 were unusually promiscuous sexually, 40 were abnormally shy with the opposite sex and 26 were misogamists. It should be noted that these findings are not necessarily confirmatory of the thesis that paranoid reactions are directly traceable to a purely sexual origin, inasmuch as examination of the individual patients and a study of their histories failed to reveal that their marital difficulties were primarily due to troubles in the sexual sphere. Sexual incompatibility, as such, was a rare complaint, whereas uncontrollable outbursts of temper, marked egocentricity, self-

2. Claude, H.: Les psychoses paranoïdes, Encéphale **20**:137 (March) 1925.

3. Bleuler, E.: Textbook of Psychiatry, translated by A. A. Brill, New York, The Macmillan Company, 1936, p. 531.

ishness, a rigid makeup, a sensitive and brooding disposition and unwillingness to discuss matters causing friction in the home were frequently mentioned. It is true, of course, that some would feel that many of these traits were merely indications of fixation at the stage of infantile psychosexuality and would draw their conclusions in accord with that opinion.

It is not surprising to note that these personality difficulties which were blamed for the many unsuccessful marriages were more common in those whose illnesses came as a gradual exaggeration of a predisposed personality, and hence that those whose conditions were diagnosed as paranoia or paranoid state showed a higher incidence of unsatisfactory heterosexual adjustments than did any of the other large groups, just as these same persons consistently demonstrated less ability to adjust well in all other kinds of social contacts.

Attention was next turned to an investigation of the prepsychotic personality, which, although made with due skepticism, born of a realization of the difficulties and inaccuracies inherent in any such study,[4] nonetheless revealed many interesting facts. For 54 patients the information concerning the early life was so sparse as to be valueless, but slightly more than a third of the group exhibited psychopathic traits or other definite evidence of maladjustment in childhood, and, as might be expected, those whose psychoses were destined to have an early onset made up the greater portion of these persons. Approximately 50 per cent of the schizophrenic patients showed such symptoms in early life, while only 14 per cent of the patients with involutional psychosis and 5 per cent of those with senile psychoses exhibited such traits. An exception to this rule was the group of those with paranoid condition, who again showed a high incidence (45 per cent) of maladjustment. The difficulties most commonly encountered in childhood were marked seclusiveness, hypochondriacal tendencies, extreme shyness, delayed sphincter control, inability to accept discipline, temper tantrums and marked compulsive traits. Perhaps even more significant than the positive findings, however, is the fact that slightly more than half the patients in the entire group had a childhood which could not justifiably be distinguished from that which is termed normal.

In puberty, too, there were a surprising number of persons whose course appeared to be no more stormy than that of the average person, and, save in those patients, chiefly schizophrenic, who were already showing prodromal symptoms of their psychoses at this early age, the presence of psychopathic symptoms was no more common than in

4. Carmichael, H. T.; Masserman, J. H., and Babcock, C. G.: Results of Treatment in a Psychiatric Outpatient Department, J. A. M. A. **113**:2292 (Dec. 23) 1939.

the earlier period of life. It was only as the adult personality pattern emerged that the more or less classic prepsychotic paranoid personality emerged. Few of the patients displayed a pattern which was typical in every respect, but 280 could be listed as showing personality traits which have been described by others as part of the prepsychotic paranoid picture, those most commonly met in this study being asocial trends, uncontrollable temper, marked projection tendencies, a suspicious or jealous nature, a rigid makeup, introspective traits, unjustified pride, inability to make concessions and a sensitive or brooding disposition.[5] Hypochondriacal symptoms were comparatively rare, being discovered in only 39 patients. In many cases, both of the functional and of the organic type, it was possible to observe the gradual exaggeration of these prepsychotic traits until they crystallized into the psychosis, either through a process of natural development or, more suddenly, as a result of some precipitating cause. More rarely it was possible to detect the presence of the symptoms prior to the definite onset of the illness, as in the case of a patient, L. K., who two years before his commitment displayed transient paranoid ideas on several occasions while under the influence of alcohol. These trends appeared in clear consciousness at a later date, when his psychosis was fully developed.[6]

Many cases were found in which there was a more or less understandable progression of symptoms, but although in a majority of the cases studied the psychosis seemed to have developed on the basis of a rather typical prepsychotic personality, there remained approximately 30 per cent of the cases in which no evidence of previous paranoid traits was betrayed and in which the psychosis came on without warning and might be said to represent unrehearsed experiments of nature. Such developments were observed in both organic and functional psychoses. As an example, there may be mentioned the case of S. M., who made an excellent adjustment throughout her early life. She was friendly, was well adjusted socially and had many wholesome interests. She appeared to be happily married and never showed any tendency toward jealousy or suspicion. Shortly after the birth of her second child, when she was 35, she began to express the belief that her food was poisoned and rapidly became so threatening toward her neighbors that commitment became imperative.

In this instance the birth of the child was regarded as the precipitating cause of the psychosis by the relatives, and it might be thought that

5. Meyer, A.: An Attempt at Analysis of the Neurotic Constitution, Am. J. Psychol. **14**:102, 1903. Kretschmer, E.: Der sensitive Beziehungswahn, Berlin, Julius Springer, 1918.

6. Freud, S.: Certain Neurotic Mechanisms in Jealousy, Paranoia, and Homosexuality, in Collected Papers, London, Psychoanalytic Press, 1933, vol. 2, p. 232.

such evidence of a precipitating factor would be comparatively common. However, in spite of the frequency with which other members of the family were prone to regard any coincidental event as an etiologic factor, it was surprising how rarely it was possible to find any vaguely plausible immediate cause for the onset of symptoms. In considerably less than a third of the cases did the relatives trace the appearance of mental symptoms to any definite event in the patient's life or environment, and many of these had to be viewed with suspicion. It is not intended to imply, of course, that no reasonable etiologic factor could be discovered in most of the cases, but merely to indicate that the time of occurrence of the mental break did not not seem to be determined by external events in the majority of cases studied. Among the more definite precipitating causes, one which appeared with great frequency was the death of a husband, parent or some one who had been the chief support, financial or otherwise, of the patient. A number of rather peculiar persons were observed who seemed to have been held within the bounds of normality chiefly because of their protected environments, only to decompensate abruptly when the stabilizing influence of a parent or a marital partner was removed. Illustrative of this may be mentioned the case of M. M., who was poorly adjusted throughout her life, having always been asocial, irritable, domineering and addicted to outbursts of temper. At the age of 16 she married a man who was 43, and her marriage appears to have been reasonably successful only because her husband treated her as a child, indulged her and even encouraged her to make unreasonable demands on him. When she was 46 her husband died, and shortly after this event her peculiar traits were more noticeable. Her interest in religion became excessive, and she finally joined a cult noted for the emotional instability of its members. Within a year she was committed to an institution because she had expressed a number of paranoid ideas, many of which were directed toward her physician.

This case also illustrates another rather common finding in the group studied. It was noticed that many who displayed only an average interest in religious matters early in their lives either tended to become fanatic in their beliefs or turned to one of the cults at about the time of onset of their other symptoms. Actually, however, there were comparatively few of those who had any religious interests whatever who were moderate in their beliefs. Whereas there were only 49 who professed or displayed an average interest in religion, that is, who were members of one of the more stable churches and attended with some degree of regularity without allowing their beliefs to color their lives too highly, there were 85 who were fanatically religious and 41 who were cultists. Two hundred and twenty-five took little or no interest in religion.

The belief in the frequency of violent action on the part of paranoid patients is so prevalent that special interest attaches to a study of the methods whereby the patients in this group attempted to deal with their difficulties. Only 56, or about 14 per cent of the group, resorted to violent action toward others. Sixty were so theatening that violence was feared, while 119, or approximately 31 per cent, found a socially acceptable method of dealing with their problems. Of this last group, 16 consulted physicians, 3 sought help from clergymen, 52 went to the police for assistance or protection, 10 applied at the hospital for commitment and 38 turned to relatives for aid against imagined persecution. The largest group of all, composed of 92 patients, took definite flight from the supposed enemies, and a few of these made suicidal attempts in an effort to escape their persecutors. Seventy-seven did nothing about the situations in which they felt themselves to be, either expressing their ideas without any accompanying action or indulging in confused episodes of socially purposeless behavior. Smaller groups were composed of 11 patients who resorted to lawsuits and 5 who indulged in alcoholic excesses, in direct contrast to their former habits. As a group, the schizophrenic patients typically took flight from the persecution, the paranoiac patients and those whose disorders were classified as a paranoid condition contributed the largest number of those resorting to legal measures, the senile patients produced a great proportion of those who resorted to violence and threats, while patients with involutional psychoses were singularly free from the use of socially unacceptable measures. It seemed possible to establish some correlation between the previous personality and upbringing of the patient and the mode of reaction to his psychosis. Thus, those who in childhood and early life had had the benefit of some training in the observance of the proprieties rarely exhibited physical violence as a part of their psychotic behavior.

Although in this respect environmental influences were important, there was little other evidence to indicate that gross environmental factors played any definite role in the development of paranoid symptoms. While misinterpretation of actual events was of rather frequent occurrence, it was only rarely that these events alone were of such a character as to make the appearance of paranoid ideas understandable or logically justifiable. Two instances of folie à deux were encountered, but in only 15 other cases was the patient subjected to the companionship or influence of any one who exhibited paranoid trends or symptoms.

Studies of the family constellations and attachments were similarly barren. Unusual attachments to individual parents or siblings were rare, and the position of the patient in the family was inconstant. Twenty-three had the role of only child, 76 were oldest in the family and 73 were youngest, while the remainder occupied intermediate positions.

As might be supposed, the time between the onset of definite symptoms and the realization on the part of relatives and friends of the need for hospitalization was variable, and ranged from a few days to as much as thirty-eight years, in the case of a seclusive patient who spent the greater part of his life in a hermit-like existence before his peculiarities became annoying to the few persons who came into contact with him. The time between the start of the illness and the commitment was greatest in the case of the patients with paranoia and paranoid conditions, whose symptoms as a rule developed gradually and did not take a bizarre form, while it was least in the case of persons with alcoholic psychoses and schizophrenia, in whom the onset was more abrupt and alarming.

An examination of the heredity of the group showed that 231, or 68 per cent, of those concerning whom there was adequate information covering at least the two preceding generations gave an absolutely negative family history. Fifty-eight showed some familial taint, 44 were the direct descendants of persons who suffered from nervous or mental disease of a type other than that characterized by paranoid symptoms, while only 8 had ancestors afflicted with a paranoid psychosis. These figures being approximately the same as those obtained in a large series of consecutive admissions of patients with all types of disorders, it was concluded that the role of heredity in paranoid psychoses was of no greater or less importance than in other types of mental disease.

An attempt was made to establish some correlation between the various factors studied and the prognosis in the case. In general, this was disappointing, for exceptions proved to be more common than rules. It was found, however, that the outcome in cases in which paranoid symptoms were displayed was more likely to be modified favorably when the delusions were not well fixed, the lack of fixity seeming to indicate that the psychosis had not yet provided the desired security. As a rule, the degree of fixity bore some relation to the age of the patient, the symptoms in young people usually being rigid only when one of the chief causes was rigid, such as deafness or repeated frustrations of a similar type. More typically, young patients entered on a psychotic pattern which was often in contrast to the previous personality and the characteristics of which changed rapidly or even disappeared entirely, whereas in older patients the delusional system most frequently appeared as the outgrowth of a personality type which had become more rigid year by year. However, the symptoms of all older patients did not prove to be rigid, and several were seen who showed rapid changes in sets of apparently well systematized delusions, evidence confirming the contention that the conflict underlying a psychosis

is not always relieved when a symptom is formed.[7] One of these, C. C., whose early history was without significance except for a quick temper and definite hypochondriacal trends, began, at the age of 49, to express the belief that his wife was unfaithful. In the course of two years many ideas of reference developed, so that every occurrence in his immediate environment took on a special meaning for him. On admission to the hospital he related a complicated series of interconnected events which had led him to the belief that he was the central figure in a plot in which some of his neighbors played an active role. In a short while he improved sufficiently to return home, and for six months he adjusted away from the hospital. He then returned voluntarily, stating that he was Christ, that he was being persecuted for the sake of mankind and that people were spying on him for the purpose of making a motion picture record of his life, starting with his birth in a manger to a virgin. At all times he was apparently receptive to suggestions that his interpretations of events might be incorrect, but as rapidly as he rejected one group of ideas another set appeared. He frequently asked the physician's advice concerning ideas which happened to come to his mind, requesting information, for example, concerning the taste of various drugs which he thought might have been placed in his food and inquiring whether it was scientifically plausible that gas could have been shot at him from a neighbor's house. In about four months he again dropped his ideas and for more than a year has been making a reasonably satisfactory adjustment at home, although insight is almost entirely lacking.

This typical character of recovery without insight was frequently encountered throughout the group and was particularly noticeable in those patients in whom the paranoid symptoms were more or less incidental features of the psychosis. One patient, I. K., had transient paranoid symptoms in connection with a manic attack. Recovery was prompt, and insight was extremely good for every aspect of her illness except the solitary paranoid trend, which, it is interesting to note, recurred in the same form in another manic attack two years later. In this connection it is worthy of comment that Bleuler's [8] contention that paranoid symptoms are most likely to appear in affective psychoses at the moment of transition between the manic and the depressive phase was confirmed in a number of instances. In almost all cases it was found that the paranoid symptoms showed marked diminution after hospitalization, possibly due to the relief of stresses inherent in life outside the institution. It appeared, in one sense, that the functional disorders with the more bizarre symptoms afforded a better prognosis

7. Freud, S.: A Case of Paranoia Running Counter to the Psychoanalytic Theory of the Disease, in Collected Papers, London, Psychoanalytic Press, 1933, vol. 2, p. 150.

8. Bleuler, E.: Affectivity, Suggestibility, Paranoia, Utica, N. Y., State Hospital Press, 1912.

than did those which were more closely related to the beliefs and actions of ordinary life, probably because the latter provided a more satisfactory compromise with the situation which was causative of the psychosis, and hence were less easily replaced. Young patients with bizarre symptoms, of course, encountered a greater risk of exhibiting subsequent deterioration, but, on the other hand, were more often seen to have an apparently complete remission than were the older patients, who, although usually less completely removed from reality, nonetheless rarely achieved anything better than a pseudoremission, accomplished by processes of evasion and "covering up."

Finally, attention was given to the probable etiologic factors in the cases studied. In the larger nosologic groups there could be found cases which were confirmatory of practically every theory which has ever been advanced concerning the etiology of paranoid reactions, but neither the group as a whole nor those belonging to a single diagnostic category could be crowded into one theoretic pigeonhole without resort to dubious intellectual processes. For example, there were 12 cases in which the psychosis was explained so adequately by the psychoanalytic conception of paranoia and the paranoid disorders [9] that no reasonable person could deny the applicability of the theory to those cases. In addition, there were perhaps three times that number to which, with only a little effort and perhaps a bit of imagination, the theory could be fitted also. But in the remainder of the cases—and the group is a large one—the psychosis defied explanation on this basis. Furthermore, well studied cases were encountered in which, although apparently the same causative processes operated as those vouched for in this theory, nonetheless psychoses entirely devoid of paranoid symptoms developed. The same can be said for other theories, and it would seem that the negative findings are at least as important as the positive evidence. To the objection that most patients in state hospitals cannot be studied thoroughly,[10] and the inevitable remark that further investigation might provide material confirmatory of one or the other theory, it is perhaps permissible to reply in the words of Janet: [11]

> With a little interpretation, displacement, dramatization, and elaboration, in conjunction with a lack of critical faculty, anything in the world can be generalized, and anything can be made into an element of everything.

Instead of one cause of paranoid symptoms there appeared to be many, of which the more common could be listed as incomplete psycho-

9. Freud, S.: Psychoanalytic Notes upon an Autobiographical Account of a Case of Paranoia, in Collected Papers, London, Psychoanalytic Press, 1933, vol. 3, p. 387.

10. Brenner, C.: On the Genesis of a Case of Paranoid Dementia Praecox, J. Nerv. & Ment. Dis. **90**:483 (Oct.) 1939.

11. Janet, P.: Psychological Healing, cited by Ross, T. A.: An Introduction to Analytical Psychotherapy, New York, Longmans, Green & Co., 1932.

sexual development, physical inferiority, impotence, deafness, blindness, the failing faculties and abilities encountered in old age, organic disease of the brain, other somatic diseases and life situations giving rise to feelings of frustration, inadequacy, anxiety,[12] insecurity, failure, shame[13] and social disorientation.[14] None of these must necessarily be taken as a complete cause in itself, but each was met at least several times as a factor which appeared to set free or exaggerate those basic paranoid mechanisms present in varying degree in every one. It is possible to say with Meyer that paranoid developments occur wherever assertion of the personality takes place on false premises, or with Bleuler that one of the requisites for the development of paranoia is the presence of a strong feeling of self opposed by some inferiority, but to say that that inferiority and those false premises are always on the same basis is not in accord with the findings of this study. That the need for assertion of the self in the face of inferiority or on false premises is also always due to the same causes is likewise doubtful.

If one final conclusion is to be drawn from this study, in addition to noting the perhaps somewhat disparate facts already reported, it must be that there are no paranoid diseases as such. Without indulging in oversimplification, it seems legitimate to consider, as a working concept, the existence of a paranoid syndrome.[15] This may appear in many settings, often arises from prepared soil and seems to develop on the basis of refusal or inability to deal acceptably with a great variety of situations. Sometimes it plays the chief role in a functional psychosis; occasionally it colors only partially, or even transiently, an illness which is organic or which is not primarily paranoid in the character of its symptoms. It appears at times as an unrehearsed attempt to achieve security, but it is also seen to develop gradually in personalities which grow more rigid year by year. Unfortunately for the ease of psychiatrists, its importance, its future course and its modifiability in each patient seem to be affected by many factors which call for study of the individual life situation.[16]

---

12. Gierlich, N.: Periodic Paranoia and the Origin of Paranoid Delusions, in Studies in Paranoia, Nervous and Mental Disease Monograph 2, New York, Nervous and Mental Disease Publishing Company, 1908.

13. Margulies, A.: Die primäre Bedeutung der Affekte in ersten Stadium der Paranoia, Monatschr. f. Psychiat. u. Neurol. **10**:265, 1901.

14. Devereux, G.: A Sociological Theory of Schizophrenia, Psychoanalyt. Rev. **26**:315 (July) 1939.

15. Lange, J.: Die Paranoiafrage, Leipzig, Franz Deuticke, 1927.

16. Friedmann, M.: Contributions to the Study of Paranoia, in Studies in Paranoia, Nervous and Mental Disease Monograph 2, New York, Nervous and Mental Disease Publishing Company, 1908. Meyer, A.: Treatment of Paranoia and Paranoid States, in White, W. A., and Jelliffe, S. E.: Modern Treatment of Nervous and Mental Disease, Philadelphia, Lea & Febiger, 1913, vol. 1, p. 614.

THE HUMAN PYRAMIDAL TRACT

III. MAGNITUDE OF THE LARGE CELLS OF THE MOTOR AREA (AREA 4)

A. M. LASSEK, M.D., PH.D.
CHARLESTON, S. C.

The present investigation is a continuation of anatomic studies on the pyramidal tract of man and is directed at a classification of the large cells of the motor cortex (area 4 of Brodmann). In spite of the fact that the cells designated as Betz or giant cells are probably the best known in the cerebral hemisphere, it is not possible to give an unequivocal description of them. As Cobb [1] said, "No definition is given as to how large a 'giant' cell has to be to deserve that name." Yet these elements, whatever their volume, are commonly said to give entire origin to the pyramidal tract fibers and thus to control isolated movements. With respect to this question Walshe [2] said:

> . . . the statement that "giant cells" alone give rise to pyramidal fibers has no meaning unless we are agreed as to what constitutes a giant cell. On examination we find that our standards on this point are various, arbitrary and without discoverable physiological value.

These same cells are also said to be responsible for the unusual excitable properties of area 4, to be larger in the leg than in the arm or head areas and, lastly, to be connected with various parts of the cortex by associational and commissural fibers. Fulton [3] expressed the belief that area 4 is a "final common path" from the cerebral cortex. If these current conceptions regarding the so-called Betz, or giant, cells are true, they merit the most detailed examination.

Since their discovery, the size of the so-called Betz cells has attracted the interest of various investigators. It is natural, therefore, that

From the Department of Anatomy, Medical College of the State of South Carolina.

1. Cobb, S.: A Preface to Nervous Disease, Baltimore, William Wood & Company, 1937.

2. Walshe, F. M. R.: On the "Syndrome of the Premotor Cortex" (Fulton) and Definition of the Terms "Premotor" and "Motor," with a Consideration of Jackson's Views on the Cortical Representation of Movements, Brain **58**:49-80, 1935.

3. Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1938.

theories have been formulated to explain this characteristic. One author stated that the larger the Betz cell the longer its axon, and another, that the larger the cell the more extensive the movement. A third stated that the larger cells connect with more internuncial neurons, and thus with more cells at lower levels, which may offer a neurologic support for the second theory. Still other factors supposed to have an influence on the volume of the nerve cell are its age and the complexity of the surrounding nerve tissue.

Although the magnitude of the so-called Betz cells has promoted these theoretic speculations, I have not been able to locate in the literature any complete or comprehensive measurements of them throughout area 4. The methods employed have been either general observations, random and scanty measurements of length and width or computation of nuclear volumes by a mathematical formula after ascertaining the diameter of the nuclei. In my hands, general microscopic observations have been untrustworthy in evaluating the bulk of a large number of cells. Measuring the length and width likewise does not give a true value, since the cells are not square or rectangular but have mostly curved surfaces, while a few have pyramidal or other forms. The determination of nuclear volumes, I believe, is a scientific approach, but the work done by this procedure involved only a restricted part of the leg area in man.[4]

MATERIAL AND METHODS

The material used was a complete serial set of pyroxylin sections through the motor cortex of man, cut sagittally from the medial surface to the lateral extremity of area 4 at a thickness of 35 microns, and stained with cresyl violet. The brain, removed one and one-half hours post mortem, was that of an apparently normal 22 year old Negress who had died suddenly as the result of an accident. Other studies have been made on the pyramidal system from the same hemisphere.[5]

The criterion for size was the area expressed in square microns. The cells were drawn by means of a camera lucida at a magnification of 800 and then measured for square area with a planimeter. Shrinkage was taken into consideration by increasing the planimetric values by 30 per cent, so that the figures given should approach normal living size.

In the fifth layer of the motor area of man there are cellular elements ranging in size from about 200 to 4,100 square microns. Among these are a relatively small number which are sharply delineated because of their larger volume and deeply staining Nissl substance. Some of these are called giant or Betz cells

4. von Bonin, G.: Studies of the Size of the Cells in the Cerebral Cortex: II. The Motor Area of Man, Cebus and Cat, J. Comp. Neurol. **69**:381-390, 1938.

5. (*a*) Lassek, A. M.: The Human Pyramidal Tract: II. A Numerical Investigation of the Betz or Gigantopyramidalis Cells of the Motor Area, Arch. Neurol. & Psychiat. **44**:718-724 (Oct.) 1940. (*b*) Lassek, A. M., and Rasmussen, G. L.: The Human Pyramidal Tract: A Fiber and Numerical Analysis, ibid. **42**: 872-876 (Nov.) 1939.

presumably because they were observed to be larger than other cortical pyramidal cells and because they simulated the anterior horn cells of the spinal cord.[6] It is not clear to me what bulk they must attain to merit the name "gigantopyramidalis." Only those larger than 900 square microns were included in this study because cells of smaller caliber begin to lose the characteristics mentioned. A total of 6,000 such cells were measured, 2,000 each in the upper, middle and lower thirds. The cells measured were not selected at random but were drawn as they appeared in the microscopic field from carefully spaced sections. The two graphs presented have been calibrated on the basis of total numbers [5a] and magnitude of cells.

Thirty groups based on size were arbitrarily made, and each cell when measured was placed in the appropriate group. For example, all the cells measuring between 900 and 1,000 square microns were cast in one group, those between 1,000 and 1,100 square microns in a second, and so on up to a maximum magnitude of 4,100 square microns. In this manner, it was possible to determine the degree of variation in area and numerically to catalogue the cells.

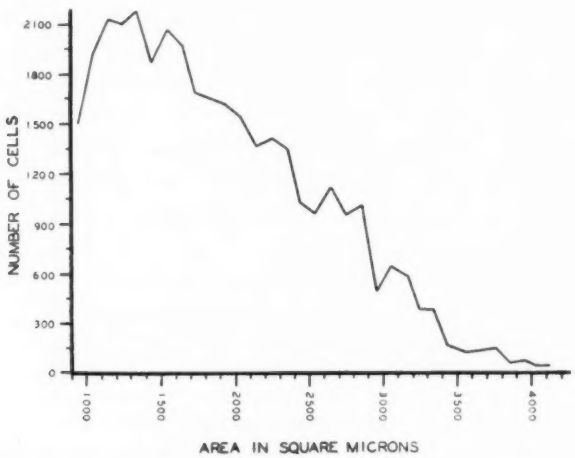


Fig. 1.—Size distribution of the large motor cells (900 to 4,100 square microns) of the fifth layer of area 4 of man graphed on the basis of the total number of such cells present.

RESULTS

The most significant finding in this study was the diversity in the caliber of the cells. Of all the cells between 900 and 4,100 square microns present in the fifth layer of area 4, there was a somewhat gradual and uniform decrease in numbers from the smallest to the largest (fig. 1).

In each third of the motor region there was a mixture of cells of various sizes, but all had a preponderance of the diminutive type.

6. Lewis, B., and Clarke, H.: The Cortical Lamination of the Motor Area of the Brain, Proc. Roy. Soc., London **27**:38-49, 1878.

Figure 2, which is a graph based on magnitude and total number of cells [5a] in each subdivision, shows that the motor leg area is the part favored by the Betz elements. The upper third had 3.4 times more of the cells under consideration than the middle, or arm, portion and 10.7 times more than the lower, or head, area. It had more cells of all sizes than the middle third, and the latter had more than the lower third. In the area allotted to head movements, no cells were found larger than 3,500 square microns.

The average area of the 6,000 cells measured was 1,757 square microns. The mean in square microns of 2,000 cells in each third of area 4 was as follows: upper, 1,978; middle, 1,702 and lower 1,592 (table). Thus, the cells in the upper third, or leg area, were 14 per

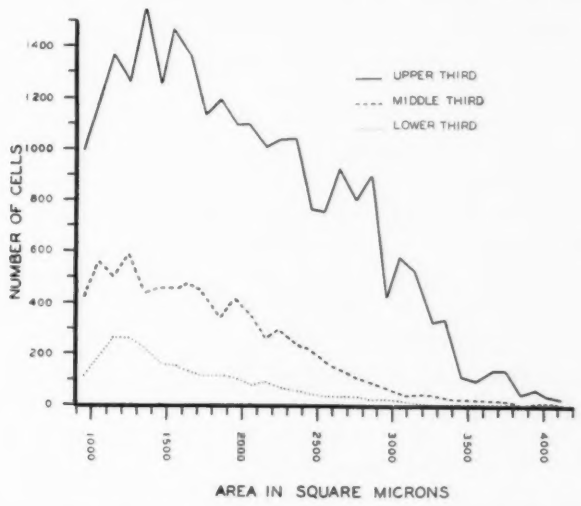


Fig. 2.—Size distribution of the large motor cells (900 to 4,100 square microns) of the fifth layer in each third of area 4 of man graphed on the basis of the total number of such cells present.

Statistical Data Showing the Average Size, Expressed in Square Microns, of 6,000 Large Motor Cells (Between 900 and 4,100 Square Microns) in the Fifth Layer of Area 4 of a 22 Year Old Negress

Region of Area 4	Number of Cells Measured	Average Area, Square Microns	Percentage *
Upper third	2,000	1,978	100.0
Middle third	2,000	1,702	86.0
Lower third	2,000	1,592	80.4
	6,000	1,757	

* The value of 1,978 square microns was considered as 100 per cent, and the other values were calculated in terms of this

cent larger than those in the middle third and 19.6 per cent larger than those in the lower third. In general, the cells were of greater average size where they were most numerous and above the point where they were buried within the central fissure, or in approximately the superior half.

COMMENT

It remains impossible for me to describe with exactness a Betz, or giant, cell in man. The only solution to this question probably would be to make wide scale, comparative measurements throughout the central nervous system, preferably in the same person. Lewis and Clarke,[6] pioneer investigators on the anatomy of the motor area, stated that the Betz cells have a close resemblance to the anterior horn cells of the spinal cord and that their size surpasses that of any class of cells in the cerebral cortex. Campbell [7] showed pyramidal cells from the paracentral portion of the postcentral gyrus as large as average-sized Betz cells in the precentral convolution. In this study, only 44 per cent of all the cells examined exceeded the average of 1,757 square microns. On this basis, the Betz elements in my specimen would number about 15,000, and consequently would be rare when one considers the motor cortex as a whole. Campbell [7] calculated there were about 25,000 Betz cells present in area 4 of man. In either enumeration, the number could not possibly account for the fibers occupying the pyramids.[8] I have not been able to separate on purely morphologic grounds the larger from the smaller cells measured. I believe, therefore, that the term Betz or giant cell is misleading and nonspecific. Since it is not known what specifically constitutes such cells, one cannot say with assurance that they give origin to all the pyramidal tract fibers. It seems to me that the cells from 900 (and perhaps less) to 4,100 square microns should have the same classification on the grounds of location and structure.

I have difficulty in harmonizing my results with the various theories pertaining to Betz cell magnitude. If the view of Lewis and Clarke [6] that the largest cells give off the longest axons were true, then the few cells which measure 4,100 square microns should be the source of axis-cylinders which course to the lowermost segments of the cord. The far greater number that measure around 1,000 square microns would give rise to fibers which, perhaps, terminate in the somatic motor nuclei in the mesencephalon, since the pyramidal tract is both corticobulbar and corticospinal. The others, between these extremes, would have an intermediate distribution. On the basis of this reasoning, most of the fibers

7. Campbell, A. W.: Histological Studies on the Localization of Cerebral Function, London, Cambridge University Press, 1905.

8. (*a*) Weil, A., and Lassek, A. M.: The Quantitative Distribution of the Pyramidal Tract in Man, Arch. Neurol. & Psychiat. **22**:495-510 (Sept.) 1929. (*b*) Lassek.[5a] (*c*) Lassek and Rasmussen.[5b]

emanating from the leg, arm or head areas would end in the brain stem and only a few in the cord.

Jackson [9] expressed the belief that large movements require large cells and small movements small cells. If extent of movement corresponds to cell magnitude, then it would be necessary to postulate that the pyramidal tract arises entirely from minute cells, since it is described as being concerned with fine, discrete movements of the digits. Acceptance of this theory would leave no role for the Betz cells in pyramidal conduction because of their large size. In order for a large cell to produce a large movement, it would need to connect below with a number of cells, possibly by means of internuncial neurons. Because of their number and bulk, the Betz cells of the leg area would make many more synaptic connections than would those of the arm or head regions. The cells would, then, be of less importance in arm innervation. Since the finer, discrete, nonstereotyped movements are well developed and specialized in the fingers of the hand, I should expect extensive pyramidal tract connections in the cervical portion of the cord. In favor of this, Weil and Lassek [8] found that approximately 50 per cent of the pyramidal tract fibers disappear in the cervical portion of the cord. Penfield and Boldrey [10] stated that in man the vertical extent of rolandic cortex devoted to the thumb is very large, while that for the leg is small. I do not believe this implies that the thumb area has more Betz cells controlling thumb movements. Quite the reverse may be true, since the thumb area is likely to be buried entirely within the central fissure, where smaller and fewer Betz cells reside, while the leg area has a much greater anteroposterior extent, where the cells are larger and more plentiful. In order for the Betz cells to have numerical significance in digital movements of the hand, it seems that the vertical extent of the hand area of the motor cortex would have to be great.

It is possible that the Betz cells vary in size according to their age. At least, one would expect them to undergo shrinkage and degenerative changes in senility. In this study, since the specimen used was that of a 22 year old Negress who died suddenly from accidental causes, the cellular sizes here reported should be representative of the normal.

I cannot make any comments in respect to Brodmann's [11] belief that the size of the Betz cells is proportional to the complexity of the sur-

---

9. Jackson, J. H.: On Convulsive Seizures (Lumleian Lectures), Brit. M. J. **1**:765-771, 1890.

10. Penfield, W., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, Brain **60**: 389-443, 1937.

11. Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, Leipzig, Johann Ambrosius Barth, 1909; cited by Hines, M.: On Cerebral Localization, Physiol. Rev. **9**:462-574, 1929.

rounding structure, as I have not had the opportunity of making comparative studies.

As to the possible role of the so-called Betz cells in pyramidal function in man, it seems logical that, because of their size, they should be related to the speed of impulses. The pyramidal tract of man arising from area 4 is known to have "fast train" connections between the cortex and the cord.[12] I believe the large cells in the fifth layer of area 4 in man, which belong to the somatic motor system as upper motor neurons, give origin to only the largest fibers of the pyramids.[5] In the pyramids of man, there are large, intermediate and small axons. Numerically and relatively, the large fibers are not abundant, but there is a close correlation between the number of so-called Betz cells (between 900 and 4,100 square microns), above, and the large fibers (over 10 microns in diameter) in the pyramids, below.[5a]

There are instances in the human nervous system in which large nerve cells concerned with innervation of striated muscle give origin to large myelinated fibers. The somatic neurons of the peripheral nervous system, for example, whether efferent or proprioceptive, have the largest cell bodies and largest myelinated fibers of any within the nerve trunks. They are the anterior horn cells and the large unipolar cells of the cerebrospinal ganglia, respectively. Such descending tracts from the brain stem as the vestibulospinal, the reticulospinal and the tectospinal possess large fibers which appear to rise from large cells. Conversely, some small cells are known to have small fibers, i. e., the pain cells. The fibers of the hypothalamico-hypophysial tract which arise from the supraoptic nucleus may be an exception to this rule, as the cells are relatively large and the axons small and mostly unmyelinated.[13] It is now a common physiologic concept that large fibers conduct more rapidly than smaller ones.[14] The larger the cross section of nerve fibers, the greater the velocity, the lower the threshold and the shorter the absolute and relative refractory period. In agreement with this view is the fact that the so-called Betz cells appear to have the lowest threshold to stimulation of any type of cells in the cerebral cortex. The impulses of these neurons may have great velocity and therefore may be important in making speedy connections with lower motor neurons. As such, they may serve to initiate movement, which Tower [15] has shown to be one of the most important functions of the pyramidal tract in the monkey.

---

12. Foerster, O.: The Cerebral Cortex in Man, Lancet **2**:309-312, 1931.

13. Rasmussen, A. T.: Innervation of the Hypophysis, Endocrinology **23**: 263-278, 1938.

14. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, Baltimore, William Wood & Company, 1937.

15. Tower, S. S.: Pyramidal Lesion in the Monkey, Brain **63**:36-90, 1940.

Probably more than any others, the investigation of Holmes and May,[16] who employed the retrograde chromatolytic method, is responsible for the belief that the Betz cells give sole origin to the pyramidal tract in man and lower ranking mammals. They examined the brains of 2 persons, 17 and 68 years of age, both of whom had transverse lesions in the seventh cervical segment. Death resulted one hundred and eight and two hundred and twenty-nine days, respectively, after accidental injury. The lesions, therefore, were not confined to the pyramidal tract alone; they were situated at some distance from the Betz cells, a condition which the authors admitted was not ideal; they did not search beyond the cerebral cortex, nor did they examine the pyramids for possible changes. If, for instance, they had compared and correlated the picture within the pyramids with that they described in the Betz cells, much more credence could be attached to the interpretation of their results. Since the pyramidal tract in all mammals is described as arising from Betz cells, it is allowable to evaluate certain recent investigations made on subhuman primates. Levin and Bradford,[17] also utilizing the retrograde chromatolytic method, found that four fifths of the corticospinal fibers in the monkey arise from area 4 and one fifth from the parietal cortex. It is interesting that these authors stated that most of the degenerating cells in their pyramidal tract center (areas 1, 2, 3, 4 and 5) disappeared twenty-eight days after hemisection of the spinal cord at the fourth cervical level. If this were true, the nerve fibers within the pyramids which arise from the disappearing cells should break down concurrently and be absorbed. Following this analysis to its conclusion, one should find within a short time (twenty-eight days, or slightly longer) after hemisection at the fourth cervical level no nerve fibers within the pyramids. The observations of Tower [15] and Davison [18] may raise doubts of the value of retrograde studies on the pyramidal tract. After making lesions in the pyramids of monkeys, Tower noticed that no retrograde degeneration occurred in the pyramidal tract immediately above the lesion. Even thirty-two months after one lesion was made, the corticospinal fibers were intact and functioning at the midpontile level. She attributed this phenomenon to the presence of collaterals which were capable of maintaining the integrity of the nerve fibers, perhaps by curtailed function. At the time of publication she did not know whether the giant cells survived the section. Davison [18] likewise in man found no demyelination in the pyradimal tract at the

16. Holmes, G. H., and May, W. P.: On the Exact Origin of the Pyramidal Tracts in Man and Other Mammals, Brain **32**:1-42, 1909.

17. Levin, P. M., and Bradford, F. K.: The Exact Origin of the Corticospinal Tract in the Monkey, J. Comp. Neurol. **68**:411-422, 1938.

18. Davison, C.: Syndrome of the Anterior Spinal Artery of the Medulla. Arch. Neurol. & Psychiat. **37**:91-107 (Jan.) 1937.

pontile level or in the peduncles after lesions in the pyramidal tract. Small nerve cells ordinarily do not show chromatolysis,[19] and, on the basis of the anatomic structure of the pyramids, I should expect small cell bodies to be responsible for the origin of a part of the pyramidal tract fibers. Therefore, there are grounds for the belief that the large motor cells may be the only ones to respond to injury of pyramidal axons.

The results of Häggqvist [20] also have an important bearing on the question of origin, since he found that area 4, and thus the so-called Betz cells, of the monkey contributed only about one fifth, and then only the largest of the fibers of the pyramids. The following statement by Levin and Bradford [17] confirms the observation of Häggqvist:

> . . . we were able to examine the brain of a rhesus monkey from which the entire frontal lobe (including the anterior wall of the central sulcus) had been extirpated 6 months previously. The bulbar pyramid was shrunken and gliosed. Stains for myelin, however, disclosed many persistent fine nerve fibers scattered throughout the pyramid, and more numerous and thicker ones in the lateral one-tenth.

All of these results, though not in agreement on some points, are suggestive of a more extensive pyramidal center than area 4.

CONCLUSIONS

There is great variability in the size of the large motor, or so-called Betz, cells in area 4 of man.

Of the cells measuring between 900 and 4,100 square microns, there is a somewhat gradual and uniform decrease in numbers from the smallest to the largest.

In each third of the motor region there is a mixture of cells of various sizes, but all have a preponderance of the diminutive type.

The upper third has more cells of all sizes than the middle portion, and the latter has more cells of all magnitudes than the lower third.

The average size of the cells measured in the upper third is 1,978 square microns, in the middle third 1,702 square microns and in the lower third 1,592 square microns.

The term Betz or giant cell is nonspecific. Therefore, it cannot be said with assurance that these cells give sole origin to the pyramidal tract fibers.

I believe the large motor cells of area 4 may be concerned with conveying speedy impulses to the lower motor neurons.

---

19. Cooper, S., and Sherrington, C. S.: Gower's Tract and Spinal Border Cells, Brain **63**:123-134, 1940.

20. Häggqvist, G.: Analysis of Fibers of the Pyramidal Tract, Acta psychiat et neurol. **12**:457-466, 1937.

PERIPHERAL BLOOD FLOW IN SCHIZOPHRENIA AND OTHER ABNORMAL MENTAL STATES

A PLETHYSMOGRAPHIC STUDY

DAVID I. ABRAMSON, M.D.

NORMAN SCHKLOVEN, M.D.

AND

KURT H. KATZENSTEIN, M.D.

CINCINNATI

The peripheral circulation in schizophrenia has recently been the subject of a number of investigations. Olkon,[1] in a study of the character of the cutaneous capillaries in a large series of schizophrenic subjects, concluded that there were a definite deficiency and typical morphologic abnormalities in this portion of the vascular bed, the severity of the disease being related to the degree of derangement. Freeman,[2] investigating circulation time in normal and in schizophrenic subjects, found that the schizophrenic group was characterized by an abnormally slow and highly variable rate of blood flow. On the other hand, Gottlieb [3] presented evidence that the circulation time was normal in this disease. Other studies on schizophrenic subjects have indicated a certain degree of dysfunction of the autonomic nervous system, as suggested by abnormal responses to exposure to cold and hot baths,[4]

From the May Institute for Medical Research of the Jewish Hospital, and the Longview State Hospital.

This study was aided by the Samuel and Regina Kuhn Fund, and by a grant from the Dazian Foundation for Medical Research.

1. Olkon, D. M.: Capillary Structure in Patients with Schizophrenia, Arch. Neurol. & Psychiat. **42**:652 (Oct.) 1939.

2. Freeman, H.: The Variability of Circulation Time in Normal and in Schizophrenic Subjects, Arch. Neurol. & Psychiat. **39**:488 (March) 1938.

3. Gottlieb, J. S.: Arm to Carotid Circulation Time in Abnormal Mental States, Arch. Neurol. & Psychiat. **41**:1117 (June) 1939.

4. Finkelman, I., and Stephens, W. M.: Heat Regulation in Dementia Praecox: Reactions of Patients with Dementia Praecox to Cold, J. Neurol. & Psychopath. **16**:321 (April) 1936. Gottlieb, J. S., and Linder, F. E.: Body Temperatures of Persons with Schizophrenia and of Normal Subjects: Effect of Changes in Environmental Temperature, Arch. Neurol. & Psychiat. **33**:775 (April) 1935.

to warm air [5] and to the intravenous administration of epinephrine.[6] According to Freeman,[7] the greater reactivity of schizophrenic subjects to cold implies a dysfunction of the neural mechanisms controlling vasoconstrictor tone, while vasodilatation may be normal. The hypofunction of the sympathetic nervous system in these patients has recently been emphasized by Gellhorn.[8]

In the present investigation, the rate of peripheral blood flow in various mental states was studied by means of the venous occlusion plethysmographic method. In this manner, readings of the blood flow for different portions of the extremities were obtained under controlled conditions.

METHOD

The study was performed on 29 patients with schizophrenia and 23 subjects with other mental diseases, including psychoneurosis, mental deficiency, chronic alcoholism, manic-depressive psychosis and dementia paralytica. Thirty-eight normal subjects, in approximately the same age group, were used as a control series. The rate of peripheral blood flow was determined in the following manner: The hand and the contralateral forearm or leg were placed in appropriately shaped plethysmographs. Each apparatus was made watertight by stretching a rubber diaphragm, through which the extremity passed, over the opening or openings in the plethysmograph, the diaphragm being held in place with a ring. A rubber cuff, an extension of the diaphragm, was attached to the skin with rubber cement, and the diaphragm was reenforced by a felt pad and two leaves of an aluminum iris diaphragm. The plethysmograph was then filled with water at a constant temperature (either 32 or 45 C.) and was connected with a recording system consisting of a Brodie bellows and a pen-writing lever. The latter recorded changes in volume of the extremity on a fast moving drum. The actual determination of blood flow was obtained by applying a pressure of about 70 mm. of mercury to the extremity, proximal to its insertion into the plethysmograph. Since this was sufficient to stop venous outflow without interfering with arterial inflow—at least for the first few seconds of application—the extremity increased in size, the rate of increase depending on the rate at which the blood entered the limb. This change in volume was recorded on the drum, and by means of water calibration of the plethysmograph the quantity of blood entering the extremity in the first second was determined. From this figure the number of cubic centimeters of blood flow per minute per hundred cubic centimeters of limb volume was calculated. In studying blood flow in the forearm or leg, a pressure of 300 mm. of mercury was maintained at the wrist or ankle during the actual determination,

5. Cameron, D. E.: Heat Production and Heat Control in the Schizophrenic Reaction, Arch. Neurol. & Psychiat. **32**:704 (Oct.) 1934.

6. Freeman, H., and Carmichael, H. T.: A Pharmacodynamic Investigation of Autonomic Nervous System in Schizophrenia, Arch. Neurol. & Psychiat. **33**: 342 (Feb.) 1935.

7. Freeman, H.: Skin and Body Temperatures of Schizophrenic and Normal Subjects Under Varying Environmental Conditions, Arch. Neurol. & Psychiat. **42**:724 (Oct.) 1939.

8. Gellhorn, E.: Effects of Hypoglycemia and Anoxia on the Central Nervous System, Arch. Neurol. & Psychiat. **40**:125 (July) 1938.

to prevent venous return from the hand or foot, as the case might be.[9] Special precautions were taken to reduce all external stimuli to a minimum, and the room temperature was maintained between 25 and 27 C. (For further details as to technic, reference may be made to previous work.[10])

In some instances the effect of arterial occlusion was studied. This was accomplished by applying a pressure of 300 mm. of mercury to the proximal portion of the extremity for a period of ten minutes. Then, on release of the pressure, readings of the blood flow were taken at ten second intervals for the subsequent five minutes, during which period a state of reactive hyperemia existed. From these readings a graph was constructed, and, by means of a planimeter, the number of cubic centimeters of excess blood flow, over and beyond the initial control level, was calculated for the duration of reactive hyperemia. This figure was then divided by the period of occlusion (ten minutes) in order to determine the number of cubic centimeters of excess blood flow for each minute of tissue ischemia.

RESULTS

Resting Blood Flow.—Before the data obtained for the patients with various types of mental disease are presented, it is necessary to establish the normal resting blood flow in the different portions of the extremities. In a series of 38 control subjects, it was found that at a bath temperature of 32 C. (i. e., the temperature of water in the pletysmograph) the blood flow in the hand was 9.7 $\pm$ 3.51 cc. per minute per hundred cubic centimeters of limb volume, in the forearm 1.8 $\pm$ 0.68 cc. and in the leg 1.2 $\pm$ 0.24 cc. At a bath temperature of 45 C., the resting blood flow in the hand was 22.6 $\pm$ 4.3 cc.

Examination of tables 1 and 2 reveals that both the schizophrenic patients and those with other types of mental disease demonstrated either a normal or an increased resting blood flow in the forearm and leg at a bath temperature of 32 C. In the hand, however, there was a definite tendency for the readings to be reduced, although a considerable variation in the individual figures existed. It is of interest to note that in those subjects who had previously received insulin treatment, the blood flow in the hand was for the most part somewhat higher than in the remaining patients (table 1).

In view of the predominantly low resting blood flow in the hand, it was thought worth while to determine whether this was due to excessive neurogenic vasoconstriction or to organic involvement of the

---

9. Grant, R. T., and Pearson, R. S. B.: The Blood Circulation in the Human Limb: Observations on the Differences Between the Proximal and Distal Parts and Remarks on the Regulation of Body Temperature, Clin. Sc. **3**:119 (April) 1938.

10. Abramson, D. I.; Zazeela, H., and Marrus, J.: Plethysmographic Studies of Peripheral Blood Flow in Man: I. Criteria for Obtaining Accurate Plethysmographic Data, Am. Heart J. **17**:194 (Feb.) 1939; II. Physiologic Factors Affecting Resting Blood Flow in the Extremities, ibid. **17**:206 (Feb.) 1939. Ferris, E. B., Jr., and Abramson, D. I.: Description of a New Plethysmograph, ibid. **19**:233 (Feb.) 1940.

TABLE 1.—*Resting Blood Flow in Patients with Schizophrenia*

Subject	Age	Sex	Blood Flow, Cc. per Minute per 100 Cc. of Limb Volume			Comment
			Hand	Forearm	Leg	
J. W.	22	M	1.3	...	0.7	
U. W.	24	M	20.5	1.4	...	
P. R.	40	M	12.2	2.1	...	
F. W.	42	F	5.6	2.4	...	
C. B.	39	M	3.3	...	...	
H. G.	18	M	6.5	1.3	...	
J. G.	40	M	...	6.9	...	
M. S.	17	M	6.1	2.0	...	
S. J.	24	M	...	...	2.0	
M. W.	36	M	1.7	0.7	...	
J. M.	35	M	3.0	...	1.6	
J. R.	23	M	6.0	...	1.4	
R. S	48	M	7.3	2.2	...	
E. G.	21	M	6.4	1.8	...	
E. C.	21	M	5.8	...	2.1	
H. R.	32	M	10.0	...	2.5	
Z. P.	40	M	9.0	...	0.5	
C. D.	54	F	2.8	2.8	2.8	
S. G.	43	F	1.7	4.9	...	
M. L.	32	F	2.8	1.2	...	
G. T.	30	M	3.7	...	1.4	
A. Z.	29	F	8.2	1.7	...	Insulin-treated
R. H.	24	M	19.3	3.5	...	Insulin-treated
D. H.	32	F	8.0	1.0	...	Insulin-treated
D. S	13	F	6.7	1.2	...	Insulin-treated
R. M.	18	M	3.8	3.3	0.9	Insulin-treated
M. R	32	M	...	2.0	2.3	Insulin-treated
C. J.	18	M	18.8	2.1	...	Insulin-treated
R. K.	23	M	7.6	...	1.0	Insulin-treated
			7.2±5.1	2.3±1.4	1.6±0.71	

TABLE 2.—*Resting Blood Flow in Patients with Other Mental Diseases*

Subject	Age	Sex	Blood Flow, Cc. per Minute per 100 Cc. of Limb Volume			Diagnosis
			Hand	Forearm	Leg	
G. G	52	M	14.2	4.1	2.4	Psychoneurosis
C. B	19	M	4.7	...	1.4	Psychoneurosis
S. L	25	M	8.9	...	0.9	Psychoneurosis
J. K	39	M	4.6	...	2.5	Psychoneurosis
H. P.	18	F	4.8	1.5	...	Psychoneurosis
L. A.	32	F	9.3	1.0	...	Psychoneurosis
S. L.	38	M	8.9	...	0.9	Psychoneurosis
I. H	38	M	2.5	0.9	...	Psychoneurosis
R. S	36	F	2.4	2.6	...	Mental deficiency
Z. S.	32	M	5.9	...	1.8	Mental deficiency
S. C.	50	M	...	2.6	...	Mental deficiency
C. W.	48	F	2.1	...	...	Mental deficiency
A. G.	35	M	...	1.8	...	Dementia paralytica
L. K	46	F	2.8	...	...	Dementia paralytica
M. S	56	F	1.1	...	...	Dementia paralytica
B. W	57	F	2.6	1.4	...	Chronic alcoholism
A. D.	40	M	4.4	...	1.6	Chronic alcoholism
J. K.	28	M	12.2	...	2.8	Chronic alcoholism
C. S	37	M	9.1	...	2.8	Chronic alcoholism
J. Z	71	M	5.4	3.3	...	Chronic alcoholism
R. R.	38	M	5.4	1.7	...	Chronic alcoholism
A. H.	71	F	1.5	...	...	Manic-depressive psychosis
K. M.	23	M	11.0	4.0	0.8	Manic-depressive psychosis
			5.9±3.5	2.2±1.0	1.9±0.7	

blood vessels. Accordingly, in a series of 9 patients in whom a reduced circulation had been previously observed in the hand the extremity was exposed to a bath temperature of 45 C., so as to produce maximal vasodilatation of cutaneous blood vessels. Under these conditions the average blood flow was 21.1 ± 8.6 cc. per minute per hundred cubic centimeters of limb volume, as compared with a control value of 22.6 ± 4.3 cc.

Response to a Period of Arterial Occlusion.—In a previous investigation on normal subjects,[11] the effect of varying periods of arterial occlusion on the subsequent rate of blood flow was studied in the different portions of the extremities. It was found that during the state of reactive hyperemia which followed the release of the pressure the number of cubic centimeters of excess blood flow to the limb bore a definite relationship to the period of tissue ischemia. It was found that at a

TABLE 3.—*Response to a Ten Minute Period of Arterial Occlusion* *

Subject	Hand	Leg	Diagnosis
Z. P.	3.2	0.6	Schizophrenia
R. K.	...	0.9	Schizophrenia
M. S.	...	1.2	Schizophrenia
J. W.	2.5	0.9	Schizophrenia
S. J.	...	0.8	Schizophrenia
G. T.	...	0.6	Schizophrenia
S. L.	3.4	0.5	Psychoneurosis
H. P.	1.9	...	Psychoneurosis
J. K.	...	0.9	Psychoneurosis
C. B.	1.8	1.0	Psychoneurosis
A. G.	2.0	...	Dementia paralytica
	2.5±0.2	0.9±0.2	

* The figures represent the number of cubic centimeters of excess blood flow per hundred cubic centimeters of limb volume (based on a minute of arterial occlusion) which entered the extremity during the period of reactive hyperemia.

bath temperature of 32 C. the number of cubic centimeters of excess blood flow for each minute of arterial occlusion was 2.1 ± 0.8 cc. for the hand and 0.9 ± 0.4 cc. for the leg. It was considered that these findings were in some way associated with the local metabolism of the tissues. In the present investigation the effect of a ten minute period of arterial occlusion was studied in a series of 11 psychotic patients. Examination of table 3 shows the results in the abnormal group to be grossly similar to those previously reported for normal subjects.

COMMENT

It has been recently demonstrated that the circulation in the hand is affected by many external and psychic stimuli. For example, a pain-

11. Abramson, D. I.; Katzenstein, K. H., and Ferris, E. B., Jr.: Observations on Reactive Hyperemia in Various Portions of the Extremities, Am. Heart J., to be published.

ful stimulus,[12] a mental problem in arithmetic,[12b] hyperventilation,[12b] inhalation of carbon dioxide [13] or a deep breath [14] will cause vasoconstriction of the blood vessels in the hand, with no effect on, or even an increase in, the blood flow to the forearm. The fact that this vasoconstrictor response is not elicited in the sympathectomized hand [15] suggests that it is dependent on the integrity of the sympathetic nervous system. The presence of numerous arteriovenous shunts in the finger tips, with their abundant supply of nerve fibrils, and the absence of these structures in the skin of the forearm, may account for the difference in the response in these vascular sites. Furthermore, it has been shown that, in contrast to the hand, the blood vessels in the forearm are little, if at all, affected by changes in sympathetic vasoconstrictor tonus under ordinary environmental conditions.[12b]

In view of these observations, it is possible that the low resting rate of blood flow, observed in the hand in the majority of the psychotic patients studied, is due to an excessive vasoconstriction of the blood vessels, particularly of the arteriovenous shunts. That this is a functional state is supported by the observation that when the extremity is exposed to a bath temperature of 45 C., the blood flow rises to a level which is as high as that found in normal subjects under similar conditions. In other words, the vasodilating effect of local heat is sufficient to overcome the existing neural vasoconstriction. The fact that the resting blood flow in the forearm and the leg was found to be either normal or increased would also be in accord with the view that there is no lesion of the blood vessels at the periphery in cases of schizophrenia or of the other mental diseases studied.

The presence of an abnormally slow circulation time in cases of schizophrenia [2] probably can be explained on the basis of the low rate of blood flow present in the hand, since Stead and Kunkel [16] have

12. (*a*) Capps, R. B.: A Method for Measuring Tone and Reflex Constriction of the Capillaries, Venules and Veins of the Human Hand with the Results in Normal and Diseased States, J. Clin. Investigation **15**:229 (March) 1936. (*b*) Abramson, D. I., and Ferris, E. B., Jr.: Responses of Blood Vessels in the Resting Hand and Forearm to Various Stimuli, Am. Heart J. **19**:541 (May) 1940.

13. Gellhorn, E., and Steck, I. E.: The Effect of the Inhalation of Gases with a Low Oxygen and an Increased Carbon Dioxide Tension on the Peripheral Blood Flow in Man, Am. J. Physiol. **124**:735 (Dec.) 1938.

14. Bolton, B.; Carmichael, E. A., and Stürup, G.: Vaso-Constriction Following Deep Inspiration, J. Physiol. **86**:83 (Jan.) 1936.

15. Steck, I. E., and Gellhorn, E.: The Effect of Carbon Dioxide Inhalation on the Peripheral Blood Flow in the Normal and in the Sympathectomized Patient, Am. Heart J. **18**:206 (Aug.) 1939. Capps, R. B.; Weiss, S., and Ferris, E. B., Jr.: Unpublished observations.

16. Stead, E. A., Jr., and Kunkel, P.: Influence of the Peripheral Circulation in the Upper Extremity on the Circulation Time as Measured by the Sodium Cyanide Method, Am. J. M. Sc. **198**:49 (July) 1939.

shown that the state of the peripheral circulation in an extremity influences the velocity of venous flow. By immersing one hand in water at 40 to 43 C. and the other in water at 23 to 30 C., these authors observed variations in circulation time which ranged from eighteen and five-tenths seconds, in the warm arm, to thirty-two and three-tenths seconds, in the cool arm. It would appear, therefore, that the difference in results obtained in schizophrenic patients by Freeman [2] and by Gottlieb [3] can be accounted for, in part at least, by the variations in blood flow in the hand observed in this group (table 1).

Our data obtained with the application of an arterial occlusion pressure suggests that the response of blood flow to tissue ischemia in patients with the various mental diseases studied is in no way different from that observed in normal subjects. Whether these observations imply that local metabolism in the extremities is normal in these conditions cannot be stated with certainty at present. The fact that the blood vessels in the extremities of the abnormal subjects dilated to the same degree as did those in the extremities of the control group is further evidence for the view that no peripheral vascular lesion is present.

SUMMARY AND CONCLUSIONS

Studies of peripheral blood flow, using the venous occlusion plethysmographic method, were made on a series of 29 schizophrenic patients and on 23 subjects with other mental diseases, including psychoneurosis, mental deficiency, chronic alcoholism, manic-depressive psychosis and dementia paralytica.

In the great majority of the psychotic patients the peripheral blood flow was markedly or moderately diminished in the hand, whereas the readings for the forearm and the leg were either normal or increased. Exposure of the extremity to local heat, so as to cause maximal dilatation of the cutaneous vessels, resulted in an increased flow in the hand which was now as great as that obtained in normal subjects under the same conditions.

Reactive hyperemia, produced in psychotic patients by the application of an arterial occlusion pressure, was similar in all respects to that observed in normal subjects.

These studies demonstrate that there is no lesion of the arterial tree at the periphery in schizophrenia or in the other mental diseases studied. The reduced blood flow observed in the hand is probably due to an excessive vasoconstrictor tonus.

The conflicting results obtained in studies on circulation time in patients with schizophrenia can be attributed, in part at least, to the variable blood flow in the hand observed in this state.

Dr. E. A. Baber cooperated in supplying the subjects used in the study, and Mrs. Robert Senior assisted in the experiments.

ENCEPHALOPATHY DUE TO BURNS

REPORT OF A CASE

NATHAN ROTH, M.D.
NEW YORK

Since a severe burn constitutes a serious trauma, attended by severe shock and offering a genuine threat to life, it is to be expected that it will leave a deep impress on the psyche of the victim, which will subsequently be reflected in his behavior. Apart from the more subtle psychologic effects, however, there is evidence that, on occasion, a burn may be the etiologic agent in the production of lesions of the central nervous system. Kruse [1] reported the case of a 14 month old child in which an extensive, second degree burn was followed by blindness, progressive hydrocephalus and mental deterioration; there was subsequent recovery from the blindness. Globus and Bender [2] reported a case of disseminated toxic-degenerative encephalopathy (disseminated sclerosing demyelination) secondary to extensive and severe burns in an 8 year old boy. This paper adds another to the short series of reported cases in which neurologic changes consequent on severe burns have been demonstrated.

REPORT OF CASE

History.—An 8 year old white girl, of Italian parentage, on April 4, 1940 was accidentally burned, when a kettle of boiling water fell on her. She sustained second and third degree burns of the entire dorsum of the trunk, the left side of the anterior thoracic wall, the right arm, the left hand and the right thigh. She was immediately admitted to another hospital in this city, where the burns were treated with tannic acid and general supportive measures, including intravenous administration of fluids, were carried out. On the day of admission the patient's condition was described as "toxic," and she vomited. During the next twelve days the temperature curve showed peaks as high as 104 F. and she had three chills. In the ensuing week her general condition was good, the burned areas were healing and granulating well and no abnormalities in the mental status were detected. On April 24, twenty days after the burns had been sustained, the patient suddenly lapsed into coma and had a series of generalized convulsions. The temperature rose to 107 F., the pulse rate to 130 per minute and the respira-

From the Psychiatric Division of Bellevue Hospital, and the Department of Psychiatry, New York University College of Medicine.

1. Kruse, F.: Enzephalitis und Amaurose nach Verbrennung, Deutsche med. Wchnschr. **54**:1039 (June 22) 1928.

2. Globus, J. H., and Bender, M. B.: Disseminated Toxic Degenerative Encephalopathy (Disseminated Sclerosing Demyelination) Secondary to Extensive and Severe Burns, J. Nerv. & Ment. Dis. **83**:518 (May) 1936.

tory rate to 70 per minute; her condition was critical. With the administration of supportive measures, the general physical condition improved, and the patient regained consciousness. It was then found, however, that she was "extremely irritable and unable to speak or recognize any objects"; in this condition she was admitted to the Psychiatric Division of Bellevue Hospital, on July 24.

The family history was essentially without significance. The patient had no history of past illness except for an attack of measles when she was 10 months old and whooping cough when she was 3 years old. She had been vaccinated at the age of 7 months. Her birth and early development had been normal in every way; she had never had convulsions prior to the present illness. Intellectually she was considered a little brighter than average, her school work had been good and in her social intercourse she displayed a pleasant personality. Her command of language had been good, and she understood both Italian and English.

On admission to Bellevue Hospital she was found to be well developed and well nourished, with healing burns in the areas already described and marked hypertrichosis of the parts of the extremities not involved in the burns. According to the method of Berkow,[3] it was estimated that approximately 30 per cent of the body surface had been burned.

Psychiatric Examination.—On examination she appeared alert and restless, and was unable to speak or to understand what was said to her. She was able to utter unintelligible sounds and to cry. She did not carry out commands put to her, although she occasionally mimicked activities carried out before her. She was exceedingly unstable emotionally and given to outbursts of crying when her nuisance value necessitated some curtailment of her activities. She was, however, easily guided and enjoyed the company of others. She was able to minister to her own bodily needs and to feed herself. There was definite evidence of impairment of the intellectual faculties; for example, although she was fascinated by a flashlight, she could not learn to put the light on by herself, even though the method was demonstrated to her. At times she would go about the ward picking up dirt in her fingers. During her stay in the hospital there was slight improvement. It was found that she understood the words "kiss me" and "bye-bye" and would act accordingly, but at the time of discharge, on August 3, there had been no further improvement in the speech function or general mental status.

Neurologic Examination.—In addition to alexia, agraphia and aphasia, there were continuous, athetotic movements of the right hand. Whereas the patient had always been right handed, she now used her left hand almost exclusively; when urged to feed herself with her right hand, the athetotic movements continued while the implement was in the hand. Except for hyperactive deep tendon reflexes, which were equal on the two sides of the body, and occasional, unsustained ankle clonus, the rest of the neurologic examination gave normal results.

Laboratory Examination.—The Wassermann reaction of the blood was negative. The red blood cell count was 5,100,000 per cubic millimeter, the hemoglobin concentration 95 per cent and the white cell count 9,200, with a differential count of 74 per cent polymorphonuclear leukocytes and 26 per cent lymphocytes. The albumin-globulin ratio was 3.4: 3.2. The nonprotein nitrogen of the blood measured 24 mg. per hundred cubic centimeters, the chlorides 479 mg., the total cholesterol 184 mg. and the cholesterol esters 111 mg. The serum bilirubin was

3. Berkow, S. G.: A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, Arch. Surg. **8**:138 (Jan.) 1924.

0.37 mg. per hundred cubic centimeters. The direct and indirect van den Bergh tests gave normal results. Levulose tolerance and bromsulphalein tests revealed normal hepatic function. Urinalysis gave negative results. Lumbar puncture revealed the spinal fluid to be under an initial pressure of 80 mm. of water, with a normal response to jugular compression. There was 1 white cell per cubic millimeter of spinal fluid; the total protein content was 30 mg. per hundred cubic centimeters; the Wassermann reaction was negative, and the colloidal gold curve was 0000000000.

Special Tests.—Pneumoencephalographic examination revealed marked hydrocephalus, with pronounced dilatation of the third and lateral ventricles, which was symmetric on the two sides of the brain. Cortical atrophy was also apparent, particularly in the frontal and parietal regions. The electroencephalographic tracings (taken by Dr. Hans Strauss) were, unfortunately, incomplete, since owing to lack of cooperation on the part of the patient, it was possible to apply only one frontal and one occipital electrode on the right side. The alpha frequency was 8 to 8.5 per second. Many 3 per second potentials with an amplitude of about 35 microvolts appeared in short series. Other slow frequencies, which did not form regular series, appeared. The record was thought to be abnormal, but the nature of the abnormality could not be definitely determined.

COMMENT

In the literature on burns, much attention has been paid to the question of toxins elaborated locally at the site of the burns and distributed throughout the body by the circulatory apparatus. The toxic symptoms of patients suffering from burns have been attributed to a large variety of supposedly poisonous substances, this feature of the problem still lacking clarity. The changes in the capillary bed and in the normal constituents of the blood, however, have been much more clearly demonstrated. Trusler, Egbert and Williams,[4] in a paper on burn shock, pointed out:

> Subsequent to a burn the capillaries in the injured areas dilate. The circulation stagnates, and blood plasma escapes through these injured capillaries into the tissue spaces . . . The escape of fluid from the capillaries becomes generalized, extending first to the liver, lungs and other parenchymatous organs and finally to all parts of the body.

They also emphasized that "the mechanism of death in so-called burn toxemia is secondary circulatory shock due to diffuse inflammation." It was in accordance with such views that Kruse [1] explained the pathogenesis of the neurologic signs in his case, pointing out that the disturbances are most easily understood as being due to cerebral edema—the chief pathologic change observed in the brain in cases of early death from burns. He pointed to the delayed onset of signs and symptoms of damage to the nervous system in his patient, which was also apparent in the case of Globus and Bender and in the case presented here, and

4. Trusler, H. M.; Egbert, H. L., and Williams, H. S.: Burn Shock, J. A. M. A. **113**:2207 (Dec. 16) 1939.

alluded to the similarities between the encephalopathy due to burns and that due to carbon monoxide poisoning. In the latter condition it is well recognized that the organic changes are largely dependent on intense cerebral hyperemia and edema.[5] Moreover, if the damage to the central nervous system in the present instance is to be attributed to the effect of a toxin, it is difficult to explain the delay in the appearance of the symptoms; a toxin would surely be elaborated in largest quantity at the time the burn was sustained and have its maximal effect at that time. The body of evidence therefore points to the significance of changes in the capillary bed and the alterations in the normal constituents of the blood consequent thereon in the pathogenesis of burn encephalopathy.

SUMMARY

An unusual case of encephalopathy due to burns is here presented, in which there were aphasia, athetosis and mental deterioration. The damage to the central nervous system is related to changes in the blood and circulatory apparatus.

5. Roth, N., and Herman, M.: Unusual Neuropsychiatric Sequelae of Carbon Monoxide Poisoning, with Report of a Case, Am. J. Psychiat. **95**:1359 (May) 1939.

INTRACRANIAL CHORDOMA

HOWARD ZEITLIN, M.D.
AND
SAMUEL A. LEVINSON, M.D.
CHICAGO

Intracranial chordomas are tumors arising from embryonic vestiges of the notochord (chorda dorsalis). Although these tumors remain a rare pathologic curiosity, they are of distinct clinical interest. Because of their usual position at the base of the brain, in the region of the sella turcica, they may simulate other tumors more commonly present in this region, such as chromophobic adenoma of the pituitary, craniopharyngioma, parasellar meningioma, dermoid cyst and carcinoma arising from the sphenoid sinus or in the nasopharynx with intracranial extension.

Chordoma was the name applied to these tumors by Ribbert,[1] in 1894. The notochord, which forms the primitive axial support of all vertebrates, extends from head to tail in the midline (Arey [2]). In later stages the primitive backbone becomes enclosed by a stiffer axial skeleton in the bodies of the vertebrae and in the basilar plate of the skull. Eventually the notochord degenerates. In adult man remnants are found as the swollen, mucoid "pulpy nuclei" of the intervertebral disks and along the original tract of the chorda in the vertebrae and in the basilar plate.

Chordomas, although found all along the vertebral column, occur most frequently at the two ends of the axial skeleton. More specifically, they are found in the sacrococcygeal region and in the basilar plate. In the latter area they may arise from the clivus Blumenbachii (dorsum sellae), or the sloping surface between the sella and the foramen magnum, which is composed of the sphenoid and occipital bones. In the aforementioned regions the chordal tissue appears to escape envelopment by cartilage or bone and enters into direct contact and relation with surrounding connective tissue (Linck [3]).

From the Department of Neurology and Neurological Surgery and the Department of Pathology, University of Illinois College of Medicine.

1. Ribbert, H.: Ueber die Ecchondrosis physaliphora spheno-occipitalis, Centralbl. f. allg. Path. u. path. Anat. **5**:457, 1894.

2. Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1937.

3. Linck, A.: Beitrag zur Kenntnis der menschlichen Chorda dorsalis im Hals- und Kopfskelet, Anat. Hefte **42**:604, 1911.

Chordomas are both benign and malignant and extensive reviews on the subject have appeared in the literature (Stewart and Morin,[4] Coenen,[5] Linck [3] and Hass [6]).

REPORT OF A CASE

History.—E. K., a white girl aged 18 years, entered the neurosurgical ward of the Research and Educational Hospitals on Dec. 13, 1938. Her complaints were those of headaches, numbness of the left side of the face, protrusion of the left eyeball and blurring of vision.

Onset.—The patient was well until August 1938, at which time she noticed numbness of the left side of the lower lip, which gradually spread to involve the entire left side of the face. She also noticed blurring of vision, especially on looking to the left. Generalized headaches developed, which early responded to analgesics. At about the same time she noted protrusion of the left eye and drooping of the left eyelid. Diplopia was frequently present on looking to the right. Glasses were fitted, but gave no relief for the difficulties in vision. The patient had not menstruated for four months prior to her entrance to the hospital, and during the month previous to her admission difficulty in swallowing, mainly of solids, was noted.

Examination.—The patient was well developed. The temperature was 99.8 F., the pulse rate 80, the respiratory rate 20 and the blood pressure 126 systolic and 76 diastolic. There was proptosis of the left eyeball, associated with slight drooping of the left eyelid. Funduscopic examination showed primary optic atrophy in the left eye and slight pallor of the disk in the right eye. Examination of the visual fields disclosed a right temporal constriction. The visual acuity of the right eye was 20/100 and that of the left eye 2/200.

Roentgenograms of the skull showed erosions of the posterior clinoid processes and some enlargement of the sella turcica, suggestive of a lesion along the base of the brain, probably associated wtih hydrocephalus. Roentgenograms of the optic canal, taken with the patient in the Goalwin position, showed apparent destruction on the left side. The impression was that of retrobulbar tumor involving the base of the brain.

Cranial Exploration.—In accordance with the preoperative diagnosis, a left transfrontal flap was turned down by Dr. Eric Oldberg. On opening the dura and the arachnoid a large amount of subarachnoid fluid was observed. The left frontal horn of the ventricle was tapped and 15 cc. of fluid removed. After separating the dura from the sphenoid ridge, the left optic nerve was found to be flattened by a bluish tumor mass which lay underneath the nerve. Because of the size and location of the tumor, surgical removal was not deemed advisable at this time, and only a small piece of tumor tissue was removed for microscopic study. The tissue was very soft and grayish. The possibility of an atypically located chromophobic adenoma was considered, and roentgen therapy was suggested.

Postoperative Course.—The patient made a fairly smooth postoperative recovery and was discharged on Jan. 26, 1938, with instructions to return for roentgen therapy.

---

4. Stewart, M. J., and Morin, J. E.: Chordoma: A Review with Report of a New Sacrococcygeal Case, J. Path. & Bact. **25**:40, 1922; **29**:41, 1926.

5. Coenen, H.: Das Chordom, Beitr. z. klin. Chir. **133**:1, 1925.

6. Hass, G. M.: Chordomas of the Cranium and Cervical Portion of the Spine, Arch. Neurol. & Psychiat. **32**:300 (Aug.) 1934.

Second Admission.—On May 28, 1939 the patient was readmitted, in a comatose state. She had been fairly well, except for paralysis of the third nerve, until she began to have generalized convulsions. These occurred every twenty-five minutes and were accompanied by foaming at the mouth and rigidity of the body.

Examination revealed the old optic atrophy on the left side, with complete paralysis of the third nerve on the same side and bulging of the left eyeball. There were complete right hemiplegia and weakness of the right lower part of the face. The patient could not be aroused by strong stimulation. She did not recover consciousness and died on June 2.

Necropsy.—Permission for necropsy was limited to examination of the head. The gross diagnosis was chordoma arising in the base of the middle cranial fossa; hemorrhage into the left cerebral hemisphere, involving the lateral ventricle, the internal capsule and the basal ganglia on that side; old surgical defect of the skull, and erosion of the sella turcica.

Gross Examination: Except for an old craniotomy wound the calvarium appeared normal. The dura in the region of the bone flap was roughened on its external surface by irregular islands of soft tissue. Beneath the dura at the base of the skull, lying in the middle cerebral fossa, was a large, ovoid, nodular tumor, measuring approximately 6 by 8 cm. in its largest diameters. The mass completely filled the interpeduncular fossa of the brain. The greater portion lay on the left side, where it surrounded the cavernous sinus and the left gasserian ganglion. It extended anteriorly along the left side of the sella turcica to the posterior surface of the greater wing of the sphenoid bone. A further anterior projection bulged slightly into the left retro-orbital space and compressed the left optic nerve, which was thinned considerably. Posteriorly, the mass extended to the petrous portion of the temporal bone. The clivus appeared roughened and pitted, and the tumor was slightly adherent to the clivus in this area. The left lateral portion of the sella turcica was eroded. The mass extended upward, displacing the central portions of the base of the brain, including the pons, the crura cerebri, the optic chiasm and the floor of the third ventricle (fig. 1). A few of the blood vessels seen at the inferior surface of the mass appeared to be incorporated in the tumor.

The brain weighed 1,180 Gm. The convolutions over the external surfaces were flattened. The pituitary gland was attached to the inferior surface of the tumor.

Sagittal section through the brain and tumor revealed the mass to be uniformly granular and light brown-gray. The tumor was lobulated and relatively avascular. One of the larger vessels coursing along its inferior surface appeared to be occluded. There were also small necrotic, hemorrhagic and cystic formations. The left lateral ventricle was completely filled with blood, and the hemorrhage extended into the left basal ganglia and left internal capsule. The subependymal tissue revealed numerous minute petechiae. The left caudate nucleus disclosed a small wedge-shaped area of softening, 10 by 15 mm. in diameter.

Sections were taken from the tumor and from various regions of the brain. Frozen, paraffin and pyroxylin sections were stained with sudan III, osmic acid and hematoxylin and eosin; by the methods of Van Gieson, Perdrau and Bodian and for mucin and glycogen.

Microscopic Examination: The microscopic appearance was fairly uniform. In general the cell structure varied with the degree of degenerative changes in the various foci. The tumor cells were predominantly closely approximated, round to polyhedral cells, with a distinct-staining cell membrane (fig. 2). The nuclei were relatively large and contained a well defined nucleolus and scattered fine chromatin granules. The ample, lightly staining, eosinophilic cytoplasm varied considerably in appearance, depending on the amount of vacuole formation. Throughout the tumor the small and large vacuoles were the most characteristic feature.

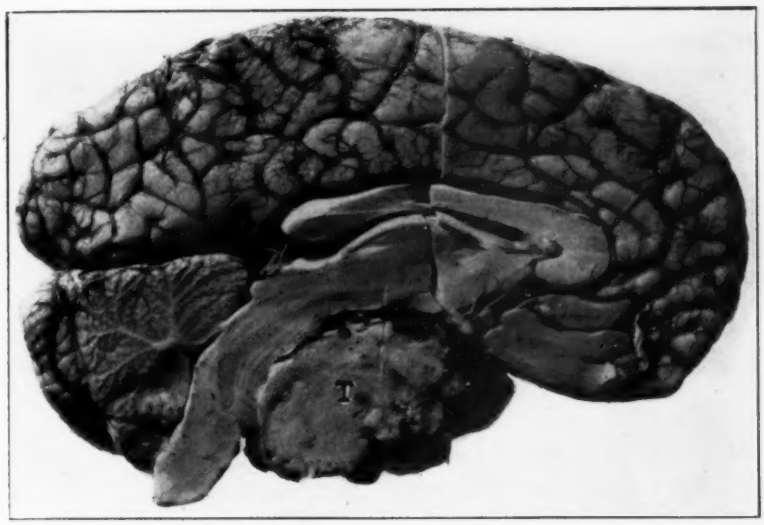


Fig. 1.—Sagittal section of the brain showing the chordoma (*T*) compressing structures at the base of the brain.

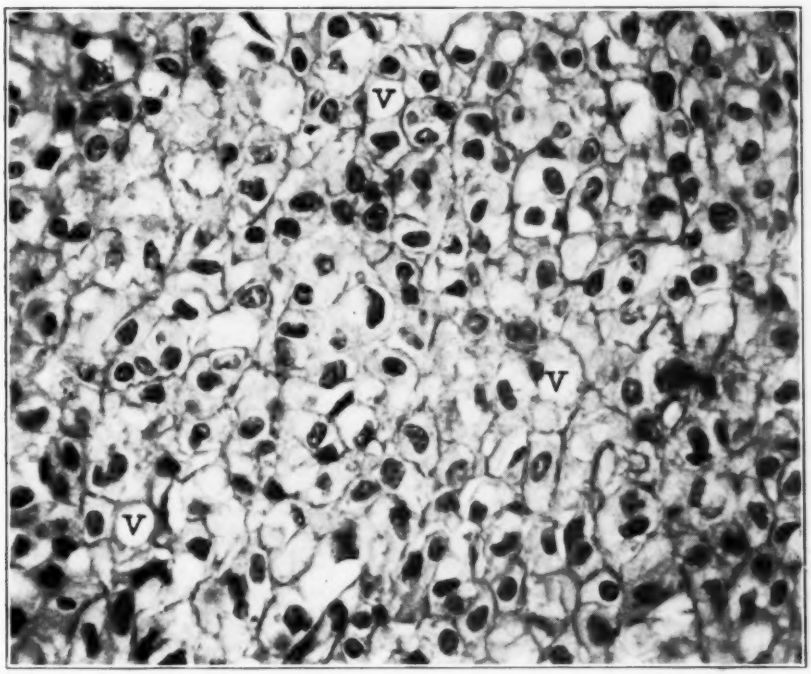


Fig. 2.—Closely approximated, round to polyhedral cells showing well defined nuclei and occasional vacuole formation (*V*). Hematoxylin-eosin stain; high magnification (from Hassin, G. B.: Histopathology of the Peripheral and Central Nervous Systems, New York, Paul B. Hoeber, Inc., 1940).

In focal areas, particularly in the vicinity of blood vessels, the cytoplasm of the cells appeared finely granular and the cells were occasionally arranged in the form of cords. In most other areas the vacuoles were single or multiple, and as they increased in size the cell membranes became distended and the nuclei were frequently displaced toward the periphery. Many of the cells appeared as "foam cells," with reticulated formations emanating from a centrally condensed cytoplasm about the nucleus of the cell. In others the vacuoles increased in size until they assumed the appearance of the so-called physaliphorous cells of Virchow (fig. 3).

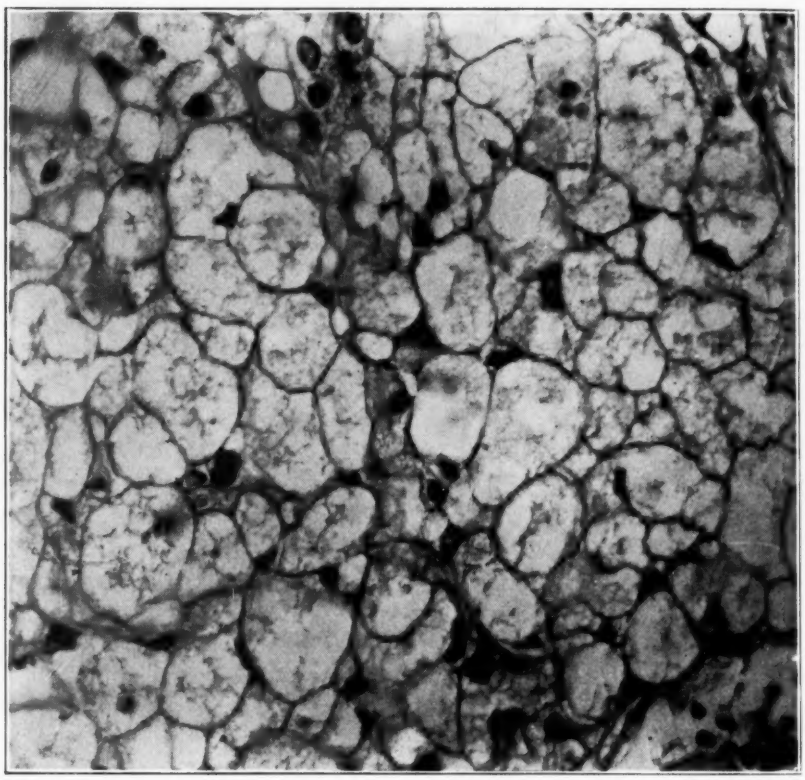


Fig. 3.—Large foam cells, or "physaliphorous cells of Virchow." The nuclei are displaced toward the periphery of the cells. Hematoxylin-eosin stain; high magnification.

Sections stained with sudan III and osmic acid showed a moderate amount of extracellular fat, which was largely distributed in areas undergoing degeneration. A few cells with intracellular globules of fat appeared to be macrophages rather than tumor cells. Frequently tumor cells scattered throughout the mass contained apparently empty vacuoles within the cytoplasm that could not be stained by methods for fat.

As the degenerative process progressed the cytoplasm disintegrated, resulting in fusion of several nuclei, which appeared as multinucleated giant cells. In areas there was a variable amount of homogeneous light pink–staining intracellular material as well as irregular extracellular deposits of a similar substance, which fused to form large circumscribed cystic areas (fig. 4). The stroma was extremely scanty

and contained few blood vessels. Mitotic figures and vacuole formation of the cell nuclei were not noted.

The tumor was surrounded by a thin capsule membrane of connective tissue containing thin-walled blood vessels. Septums arising from the capsule dipped down into the tumor, forming incomplete lobules. At the base the capsule appeared to fuse with the leptomeninges. In this region a small focus of osteoid-like tissue, as well as granular calcium deposits, a small nest of arachnoid cells and pigment-laden histiocytes, were observed.

Thrombosis of the blood vessels in the tumor and perivascular accumulations of plasma cells and small lymphocytes were noted as secondary features. The

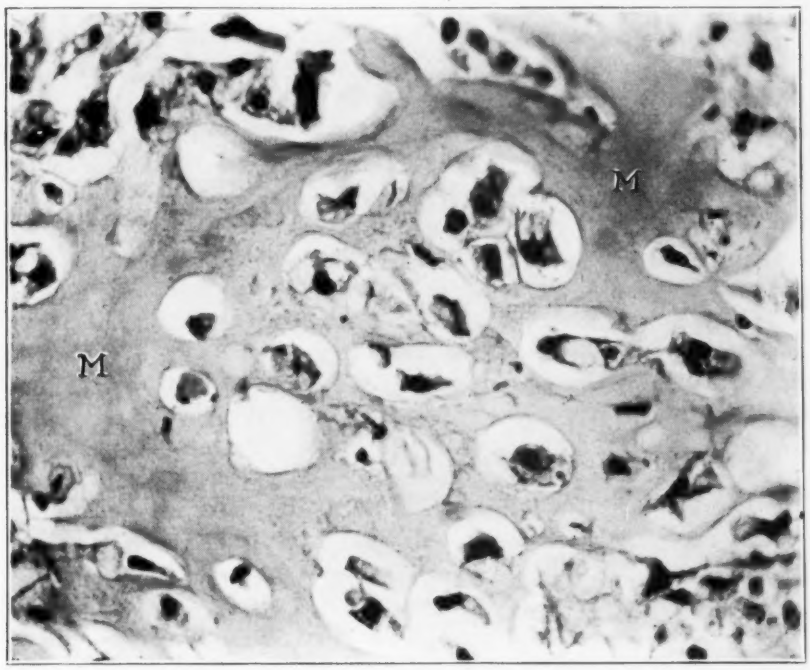


Fig. 4.—Small groups of tumor cells embedded in a homogeneous mucoid matrix (*M*).

brain tissue adjacent to the tumor revealed numerous perivascular ring hemorrhages that extended for a considerable distance into the parenchyma of the brain.

The pituitary was partially surrounded by the tumor mass. Its anterior lobe appeared normal, and the capsule was intact.

COMMENT

Virchow,[7] in his routine autopsy work, first noted a small outpouching of a gelatinous tumor attached to a small defect in the bone in the region of the clivus. He expressed the belief that benign tumors of this type were related to degenerated cartilage and called the condition "ecchon-

7. Virchow, R.: Ueber die Kretinin-Physiognomie, Verhandl. d. phys.-med. Gesellsch. in Würzburg **8**:24, 1857.

drosis physaliphoria spheno-occipitalis." In some instances the small tumors lay in the subdural space beneath the pons. Growths of the latter type are in themselves without clinical significance but are of importance as the possible starting point of a chordoma.

Müller,[8] in 1858, on the basis of embryologic studies, first pointed out the relation between these tumors and notochordal tissue. But conclusive evidence was not shown until Ribbert, in 1894, punctured the intervertebral disks in rabbits and produced benign tumors which were microscopically similar to the chordomas.

Malignant chordomas originate from notochordal cells which have preserved their early embryonic character. They are characterized by slow expansile growth, infiltration and destruction of bone, infrequent invasion of the soft tissues and frequent recurrence after excision. They only rarely metastasize. The malignant growths may project either upward into the intracranial cavity from the clivus Blumenbachii or downward into the nasopharynx, through the craniopharyngeal foramen, and, as in our case, may extend anteriorly to bulge into the retro-orbital space. The tumor may also extend posteriorly through the foramen magnum into the spinal canal (Schwyzer[9]).

The histologic evolution of the notochord and the varying microscopic picture of the chordoma have been studied in great detail by Alezais and Peyron[10] and by Linck. In general the histologic features of the chordoma partially reduplicate the morphologic features of the chorda dorsalis during its stages of evolution. Three stages have been defined: the first, of nonvacuolated, polygonal epithelial cells; the second, of marked vacuole formation, and the third, or syncytial phase, of intercellular accumulation or mucoid matrix formation. The last stage is usually seen in the adult type of chordal tissue. Linck differentiated a stage in which the cytoplasm of the cells has undergone thready changes with the production of fibrils. The latter, although observed only in a few cases, were said to resemble neuroglia fibrils (Peers[11]).

The contents of the vacuole formations have been shown to contain unstainable material, glycogen (Bailey and Bagdasar[12]) or a mucinous substance. Since in our case the tumor tissue had not been properly fixed in alcohol, the nature of the substance in the vacuoles could not be ascertained.

---

8. Müller, H.: Ueber das Vorkommen von Resten der Chorda dorsalis bei Menschen nach der Geburt und über ihr Verhältnis zu den Gallertgeschwülsten am Clivus, Ztschr. f. rat. Med. **2**:202, 1858.

9. Schwyzer, A.: A Case of Chordoma with a Hitherto Unobserved Intraspinal Extension, Minnesota Med. **20**:15, 1937.

10. Alezais and Peyron: Sur l'histogenèse et l'origine des chordoms, Compt. rend. Acad. d. sc. **174**:419, 1922.

11. Peers, J. H.: Spheno-Occipital Chordoma, Am. J. Cancer **32**:221, 1938.

12. Bailey, P., and Bagdasar, D.: Intracranial Chordoblastoma, Am. J. Path. **5**:429, 1929.

A review of previously reported cases reveals the occurrence of the more frequent clinical signs referable to multiple palsies of the ocular nerves; increased intracranial tension; failing vision; changes in the visual fields, and occasional signs of involvement of the pyramidal tracts. The unilateral exophthalmos in our case was due to an anterior extension of the tumor into the retrobulbar space.

The diagnostic feature of greatest value has been the presence of a midline area of destruction of bone extending from the region of the sella turcica to the foramen magnum. Sosman, in a personal communication to Van Wagenen,[13] pointed out a characteristic V-shaped notch in the basilar plate as an almost certain sign. The deformity is undoubtedly due to the destruction of the bone by a tumor. The roentgenographic findings and the symptoms of compression of the brain stem without marked signs of pituitary derangement should lead the neurologist to suspect the possibility of a chordoma arising from the clivus. A definite diagnosis is difficult, however, without biopsy of the tumor tissue.

TREATMENT

When these tumors reach a fairly large size, as in our case, there is a tendency to include large blood vessels in the sellar region, thereby making the surgical approach extremely difficult. On the other hand, a small, encapsulated, noninvasive tumor, when diagnosed early, might be irradicated by excision. With the advance of neurosurgical technic more tumors within the skull, formerly considered inaccessible, are being attacked radically. Van Wagenen suggested a surgical procedure for a possible approach to and removal of these tumors and expressed the belief that one is justified in removing as much of the tumor as possible in order to prolong life.

High voltage roentgen therapy, although given in our case, was of insufficient amount to permit microscopic determination of the effect of roentgen rays on these growths. The reports in the literature are also meager.

CONCLUSIONS

A case of intracranial chordoma arising from the clivus Blumenbachii with anterior extension into the retro-orbital space, causing unilateral proptosis, is reported.

The histologic features of the chordoma partially reduplicate the morphologic features of the chorda dorsalis during its stages of evolution.

Malignant infiltrating chordomas at the base of the brain have a tendency to include large blood vessels, thereby making surgical removal difficult. On the other hand, small, encapsulated, noninvasive chordomas might be eradicated by excision.

13. Van Wagenen, W. P.: Chordoblastoma of the Basilar Plate of the Skull: Suggestions for Diagnosis and Surgical Treatment, Arch. Neurol. & Psychiat. **34**:548 (Sept.) 1935.

THE PILOCARPINE SWEATING TEST

I. A VALID INDICATOR IN DIFFERENTIATION OF PREGANGLIONIC AND POSTGANGLIONIC SYMPATHECTOMY

OLAN R. HYNDMAN, M.D.
AND
JULIUS WOLKIN, M.D.
IOWA CITY

There has been some disagreement concerning the effect of pilocarpine on the sweat gland following degeneration of its postganglionic neuron. Brown and Adson [1] gave pilocrapine to 4 subjects after lumbar and dorsal ganglionectomy, and visible sweating was induced in the areas which were usually dry. They stated:

> This is evidence that degeneration of the sympathetic nerve-endings in the sweat glands had not occurred within the periods of the postoperative observations.

Lewis and Landis,[2] on the contrary, stated:

> It is quite clear that pilocarpine is capable of inducing sweating, and free sweating, in man after degeneration of the sympathetic nerves, and that it cannot be relied upon to mark the boundaries of sympathetic nerve lesions.

After cervicodorsal ganglionectomy List and Peet [3] obtained pilocarpine sweating of the ipsilateral part of the face. They explained this by assuming that cholinergic fibers course through certain cranial nerves to innervate cutaneous vessels. Pilocarpine or mecholyl (acetylbetamethyl choline) acts on the cholinergic endings of such fibers and causes the release of sufficient acetylcholine to activate the neighboring denervated sweat glands. Their tests were done, however, nine days to two

From the Department of Surgery, Neurosurgical Service, State University of Iowa College of Medicine.

1. Brown, G. E., and Adson, A. W.: Physiologic Effects of Thoracic and Lumbar Sympathetic Ganglionectomy or Trunk-Section, A. Research Nerv. & Ment. Dis., Proc. (1928) **9**:721-765, 1930.

2. Lewis, T., and Landis, E. M.: Some Physiological Effects of Sympathetic Ganglionectomy in the Human Being and Its Effect in a Case of Raynaud's Malady, Heart **15**:151-176, 1930.

3. List, C. F., and Peet, M. M.: Sweat Secretion in Man: III. Clinical Observations on Sweating Produced by Pilocarpine and Mecholyl, Arch. Neurol. & Psychiat. **40**:269-290 (Aug.) 1938.

weeks after cervicodorsal ganglionectomy. Guttmann and List [4] expressed the opinion that the preservation of pilocarpine sweating after cervical sympathetic ganglionectomy was evidence of double innervation of the sweat glands of the face.

Gask and Ross [5] stated:

> To test the sweating mechanism it has been customary in the past, following the teaching of Horsley, to inject pilocarpine, and by examining for the absence of sweating to discover the extent of the denervated area. It has been shown by Adson and Brown as well as by Lewis, that pilocarpine can induce sweating in an area completely deprived of its sympathetic supply, presumably because the drug acts directly upon the sweat glands. It is therefore fallacious to use this method as a test for sympathetic denervation.

Horsley [6] stated that pilocarpine caused no sweating below the level of a severe injury to the cord. He expressed the belief that this was a result of disuse. Langley [7] stated:

> It is clear from the course taken by the secretory fibers that the level of the non-secreting skin can only in special cases correspond with the level of the cord injury, but an absence of secretion somewhat below the level of cord injury has been confirmed.

Burn, in an unpublished communication, cited by Langley [7] reported that he found no secretion on the cat's paw some weeks after section of a sciatic nerve when pilocarpine was injected subcutaneously in the body region. Langley obtained decreased secretion in the paws of cats after section of the sciatic nerve, but even after thirty-eight days he obtained secretion when pilocarpine was injected into the gland-bearing area. He expressed the belief that the normal excitability of the gland varies considerably and that results after the nerves were cut should be correlated with the degree of original excitability.

Again, Burn [8] and Langley and Anderson [9] expressed agreement that pilocarpine may cause sweating after destruction of the nerve supply. They stated that degeneration of a mixed nerve decreases pilocarpine

---

4. Guttmann, L., and List, C. F.: Zur Topik und Pathophysiologie der Schweiss-Sekretion, Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:504-536, 1928.

5. Gask, G. E., and Ross, J. P.: The Surgery of the Sympathetic Nervous System, Baltimore, William Wood & Company, 1934.

6. Horsley, V.: Diseases of the Vertebral Column and Compression-Paraplegia, in Allbutt, T. C., and Rolleston, H. D.: A System of Medicine, New York, The Macmillan Company, 1910, vol. 7, pp. 571-584.

7. Langley, J. N.: The Secretion of Sweat: I. Supposed Inhibitory Nerve Fibers on the Posterior Nerve Roots; Secretion After Denervation, J. Physiol. **56**:110-119, 1922.

8. Burn, J. H.: The Relation of Nerve Supply and Blood Flow to Sweating Produced by Pilocarpine, J. Physiol. **56**:232-247, 1922.

9. Langley, J. N., and Anderson, H. K.: On Autogenetic Regeneration in the Nerves of the Limbs, J. Physiol. **31**:418-428, 1904.

sweating but degeneration of sympathetic nerves results in increased sweating. It is thus inferred that degeneration of sensory fibers are responsible for decreased pilocarpine sweating.[10] On the basis of this conclusion and of the assumption that disturbance of sensation by lesions of the cord may disturb pilocarpine sweating, Craig [11] studied a number of patients with lesions of the cord. He concluded that the pilocarpine sweat mechanism was disordered by lesions of the cord and that there was some correlation between diminished sweating and diminished sensibility.

We present the following cases as evidence that if sufficient time is allowed to elapse after a postganglionic sympathectomy, pilocarpine anhidrosis will agree precisely with the thermoregulatory anhidrosis and that as long as the postganglionic neuron remains intact (over two years in 1 of our cases), pilocarpine will stimulate free sweating.

METHOD

The starch-iodine sweat indicator of Minor [12] was used to differentiate sweating from nonsweating zones. In carrying out the thermoregulatory sweating test, the nude body was subjected to a temperature of at least 120 F. until the degree of sweating appeared to have reached a maximum. Great care was taken not to allow the zones of the skin in question to be in contact with anything and not to allow two cutaneous surfaces to touch each other. This requirement can be nicely fulfilled for all parts, except possibly the axillas. We feel that sweating which occurs on skin that is covered or in contact with other cutaneous surfaces cannot be accepted as indicating neurogenically or chemically induced activity of the sweat glands.[13]

The pilocarpine sweating test was carried out at room temperature. One-fifth grain (0.013 Gm.) of pilocarpine hydrochloride was injected hypodermically. The maximum response was usually obtained in from twenty to thirty minutes. We have repeated this test on the same patient under the same circumstances with and without prostigmine methylsulfate. It has been our impression that so far as sweating is concerned, prostigmine has little, if any, influence on the activity of pilocarpine. We have not used mecholyl to induce cholinergic responses.

---

10. List and Peet [3] showed that degeneration of a peripheral mixed nerve results in pilocarpine anhidrosis. They expressed the belief that the anhidrosis is not due to the degeneration of the sympathetic fibers contained in the nerve.

11. Craig, C. B.: A Study of the Sweating Reaction Induced by the Administration of Pilocarpine in Diseases of the Spinal Cord: An Aid in Localizing the Segmental Level of Spinal Cord Neoplasms, A. Research Nerv. & Ment. Dis., Proc. (1928) **9**:569-586, 1930.

12. Minor, V.: Eines neues Verfahren zu der klinischen Untersuchung der Schweissabsonderung, Deutsche Ztschr. f. Nervenh. **101**:302-308, 1927.

13. Hyndman, O. R., and Wolkin, J.: Sweat Mechanism in Man: Study of Distribution of Sweat Fibers from Sympathetic Ganglia, Spinal Roots, Spinal Cord and Common Carotid Artery, Arch. Neurol. & Psychiat. **45**:446-467 (March) 1941.

REPORT OF CASES

Postganglionic Sympathectomy.—CASE 1 (R. McG.).—The inferior cervical and upper six dorsal ganglia were removed on the left side in an attempt to alleviate left-sided migraine. A thermoregulatory sweating test revealed anhidrosis of the left side of the face and chest down to the seventh dorsal segment and of the left upper extremity. A pilocarpine sweating test one hundred and nineteen days after

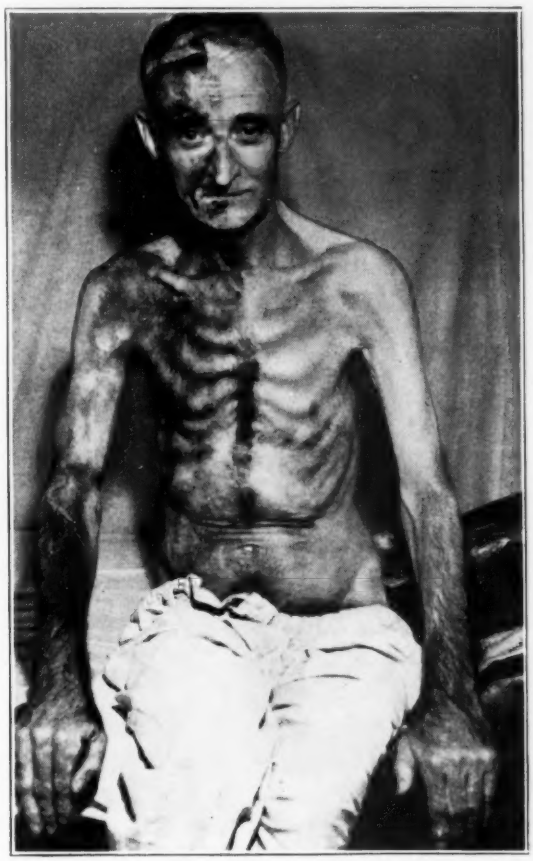


Fig. 1 (R. McG., case 1).—Pilocrapine sweating test one hundred and nineteen days after removal of the inferior cervical and upper six dorsal ganglia on the left. There is anhidrosis in the distribution of the removed ganglia which corresponds with the zone of thermoregulatory anhidrosis except for a small patch of sweating on the radial side of the wrist.

operation revealed identical anhidrosis except for a patch of sweating 5 by 2 cm. on the radial aspect of the wrist (fig. 1).

CASE 2 (E. P.).—The inferior cervical and upper three dorsal ganglia were removed on the left side for amputation stump pain. Thermoregulatory and pilocarpine sweating tests fifty-one days after operation revealed identical areas of anhidrosis (fig. 2).

CASE 3 (M. B.).—The inferior cervical and upper three dorsal ganglia were removed on the left side on Dec. 15, 1938 for relief of atypical neuralgia of the face. The inferior cervical and upper two dorsal ganglia on the right were removed on Dec. 18, 1940. A pilocarpine sweating test seven and a half months and a thermoregulatory sweating test eight months after the last operation revealed identical areas of anhidrosis (fig. 3 *A* and *B*).

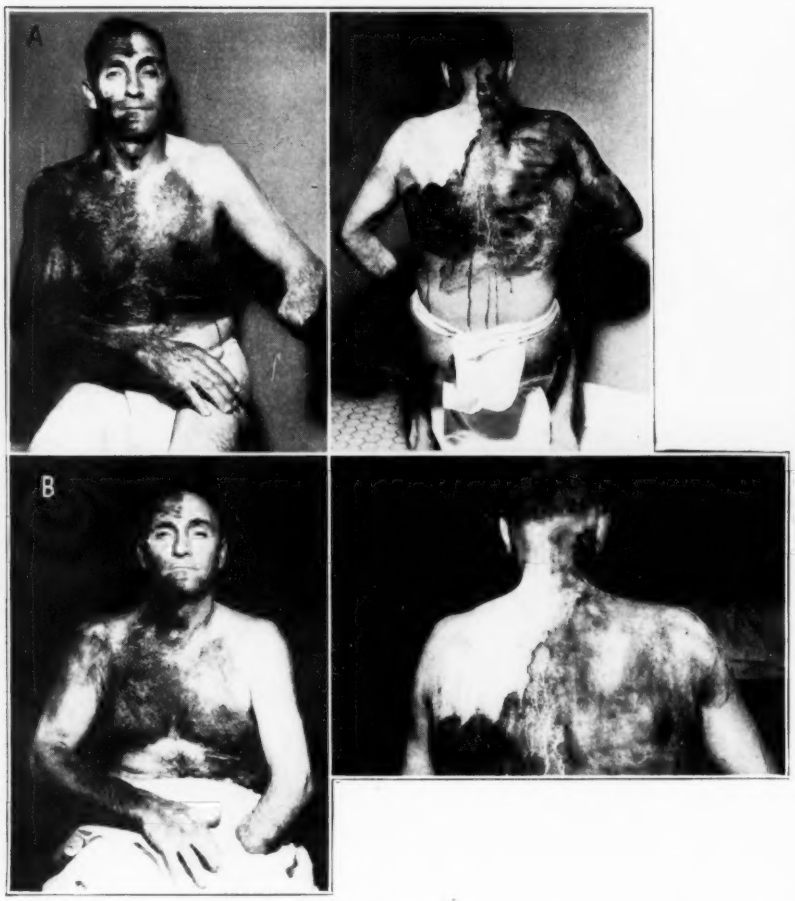


Fig. 2 (E. P., case 2).—*A*, thermoregulatory sweating test (front and back views), revealing the zone of anhidrosis fifty-one days after removal of the inferior cervical and upper three dorsal ganglia on the left. The dark shadow on the anterior wall of the chest (left side) is due to hair, and not to sweat.

B, pilocarpine sweating test (front and back views), revealing the zone of anhidrosis fifty-one days after operation. If one compares the back view with the correspondnig view in *A*, it can be seen that the pattern is identical in the two tests, even to the scattered sweating points just mesial to the left axilla.

CASE 4 (G. T.).—The inferior cervical and upper two dorsal ganglia were removed bilaterally for atypical neuralgia of the face. The operator was not certain that he had removed the second dorsal ganglion on the right, and probably did not, as indicated by the sweating test. Thermoregulatory and pilocarpine sweating tests done one year after operation revealed identical areas of anhidrosis (fig. 4 *A* and *B*).

Preganglionic Sympathectomy.—CASE 5 (H. E.).—Bilateral section of the anterior and posterior roots from the first to the fifth thoracic, inclusive, and partial bilateral chordotomy at the third thoracic level were performed for essential hypertension. A thermoregulatory sweating test one month after operation revealed

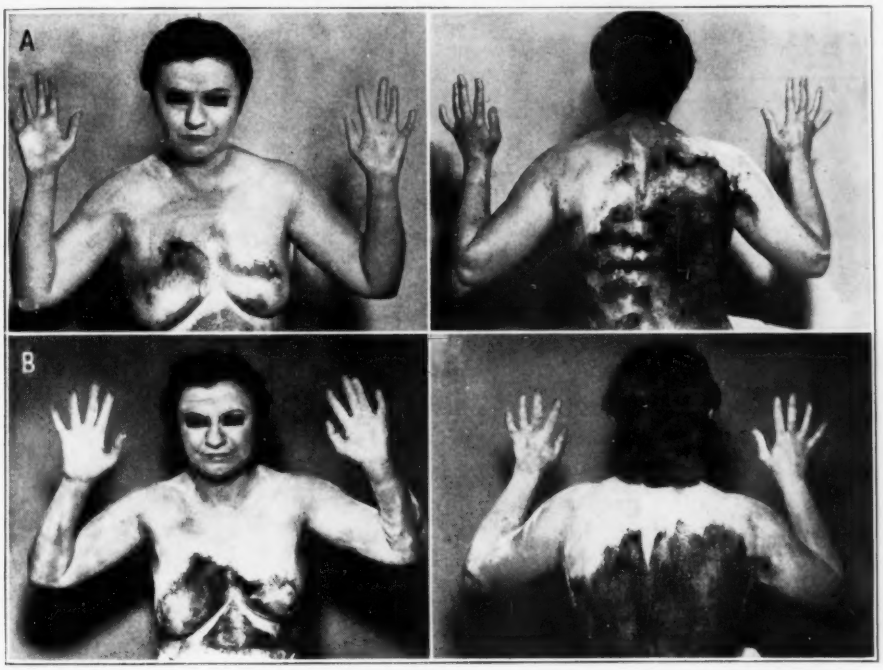


Fig. 3 (M. B., case 3).—*A*, pilocarpine sweating test (front and back views) seven and a half months after the last stage of a complete bilateral cervicodorsal ganglionectomy. There is complete anhidrosis above the second dorsal segment, inclusive, on the right and above the third dorsal segment, inclusive, on the left.

B, thermoregulatory sweating test (front and back views) eight months after the last stage of a complete bilateral cervicodorsal ganglionectomy. There is complete anhidrosis above the second dorsal segment, inclusive, on the right and above the third dorsal segment, inclusive, on the left. The marginal patterns are identical with those seen after the pilocarpine test shown in *A*.

almost complete anhidrosis of the face (fig. 5 *A*). A pilocarpine sweating test fourteen months after operation revealed free sweating over the face (fig. 5 *B*). The thermoregulatory test at this time gave the same result as before.

Case 6 (E. R.).—Section of the right splanchnic nerves and removal of the right first and second lumbar ganglia were done on Sept. 19, 1938 for essential hypertension. Bilateral section of the anterior and posterior roots from the first to the fifth thoracic, inclusive, was performed on Nov. 14, 1938. A pilocarpine sweating test two years after the last operation induced abundant sweating on the forehead and lips (fig. 6 *A*). (No sweating appeared over the abdomen or lower extremities.) A thermoregulatory sweating test, done a few days later, resulted in anhidrosis of the face except for a few beads of sweat on the left

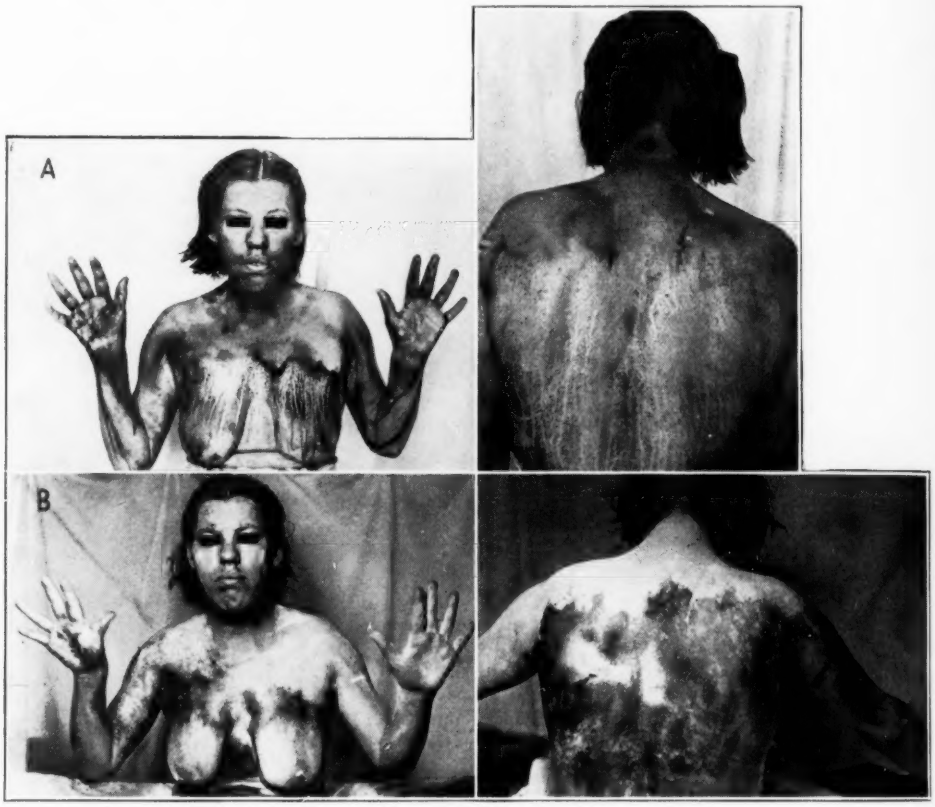


Fig. 4 (G. T., case 4).—*A*, thermoregulatory sweating test (front and back views) one year after removal of the inferior cervical and upper two dorsal ganglia on the left and of the inferior cervical and first dorsal ganglion on the right. There was some sweating on the right upper extremity, but the appearance of moisture on the left upper extremity is an artefact. The sweat has washed away much of the starch on the back, but the margin between wet and dry skin can be seen.

B, pilocarpine sweating test (front and back views) revealing an anhidrosis that is identical with that seen in *A*. The patterns on the front and back are identical in the two tests.

side of the upper lip (fig. 6 *B*). This test did not differ in result from a thermoregulatory test done shortly after the second operation. The right leg revealed anhidrosis from just below the knee down.

Combined Preganglionic and Postganglionic Sympathectomy.—CASE 7 (L. C.).—First Operation (March 13, 1939): Section of the anterior and posterior roots from the first to the fifth-thoracic, inclusive, and a partial bilateral chordotomy at

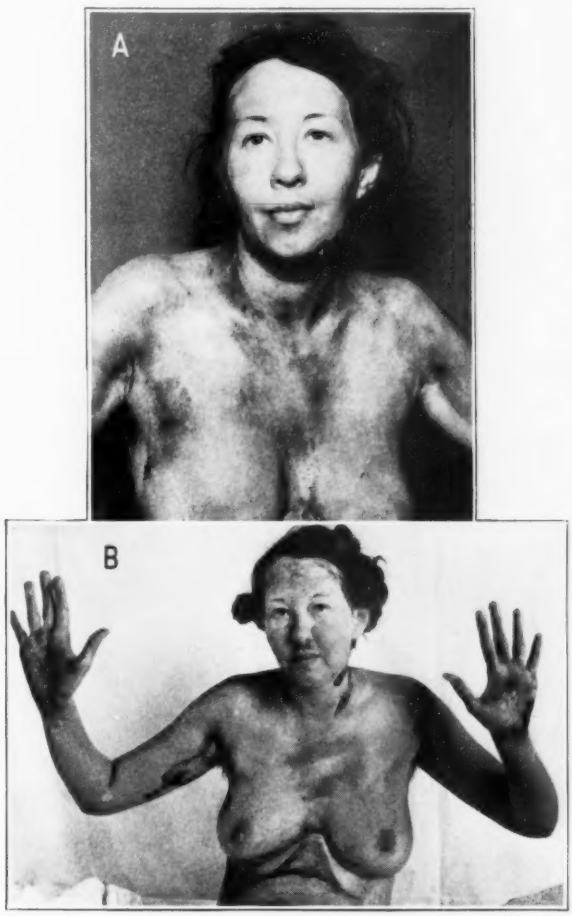


Fig. 5 (H. E., case 5).—*A*, thermoregulatory sweating test one month after a section of the anterior and posterior roots from the first to the fifth thoracic, inclusive, bilaterally. There is anhidrosis of the face except for a few small beads of sweat above the upper lip and below the lower lip.

B, pilocarpine sweating test fourteen months after operation. There is good sweating on the forehead and upper lip. (On another occasion there was even more profuse sweating of the face.)

the third thoracic level were done for essential hypertension. A thermoregulatory sweating test forty-six days after operation revealed anhidosis of the face (fig. 7 *A*).

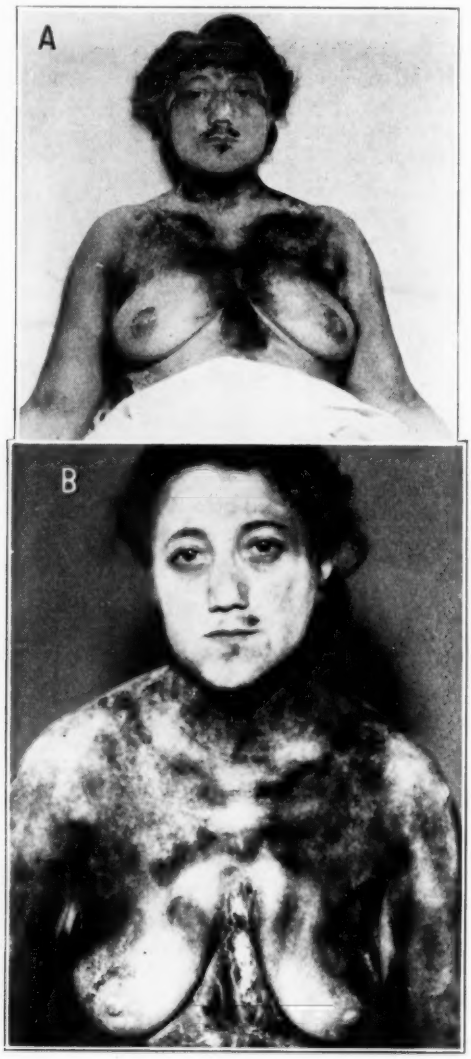


Fig. 6 (E. R., case 6).—*A*, pilocarpine sweating test two years after section of the anterior and posterior roots from the first to the fifth thoracic segment, inclusive, bilaterally. There is abundant sweating on the forehead and lips (preganglionic sympathectomized zone).

B, thermoregulatory sweating test done a few days after the pilocarpine test. There is anhidrosis of the face except for a patch on the left side of the upper lip. This result was identical with that of a thermoregulatory test done shortly after the operation.

Second Operation (Jan. 19, 1940): A cervicodorsal ganglionectomy (inferior cervical and first dorsal) on the right was performed in an attempt to relieve hyperesthesia of the right shoulder. A thermoregulatory sweating test four months after the second operation revealed the usual anhidrosis on the right[14] (fig. 7 *B*). On the left the sweating response corresponded to that shown in figure 7 *A*. A pilocarpine sweating test done three and a half months after the second operation revealed anhidrosis on the right the area of which was identical with that in the thermoregulatory test. On the left some sweating occurred on the face (fig. 7 *C*). In this case a postganglionic sympathectomy to the right side of the face and a preganglionic sympathectomy to the left side were done.

COMMENT

As a result of our studies we are convinced of two facts in relation to pilocarpine sweating: first, that as long as the postganglionic neuron is intact pilocarpine will cause sweating by peripheral action and, second, that if sufficient time is allowed to elapse after a postganglionic section pilocarpine hydrochloride, given hypodermically in $\frac{1}{5}$ grain doses, will fail to stimulate sweating in the postganglionic-sympathectomized zone. The time required for this state to develop varies, but we feel that a minimum of two months should be allowed. Ultimately the zone of pilocarpine anhidrosis agrees precisely with the zone of thermoregulatory anhidrosis. There may be an occasional point or two of pilocarpine sweating in the anhidrotic zone, but for all practical purposes this statement is true.

We agree that pilocarpine sweating may be increased shortly after postganglionic sympathectomy. As time goes on, however, the response will diminish until anhidrosis is complete, in about two months. We believe that the increased response during the early days following sympathectomy is due to the fact that the central connections have been interrupted and the existing inhibition of sweating rendered inactive,[15]

14. It will be noted that only the inferior cervical and first dorsal ganglia were removed in this case, but the result with regard to the upper extremity agrees essentially with that when the second dorsal ganglion is included. We have found this to be true in some cases and not in others. The result probably depends on variations in gray rami from the second ganglion to the brachial plexus and on whether such rami are or are not interrupted at the time of operation.

15. We feel that this observation in itself is strong evidence that sweating may be centrally inhibited. Postoperative hyperthermia is characterized by extreme vasoconstriction in the skin, producing cold extremities, absence of sweating and at times waves of pilomotor response. It appears that such a reaction is due to overactivity of the central heat-conserving mechanism. We have found it extremely difficult to initiate pilocarpine sweating in cases of such hyperthermia and believe that the failure is due to the difficulty of pilocarpine breaking through the central inhibition of sweating. By the same reasoning, it is our opinion that the pronounced vasoconstrictor action of epinephrine on the sympathectomized cutaneous vessel is only an expression of the normal influence of epinephrine, uninhibited by central impulses.

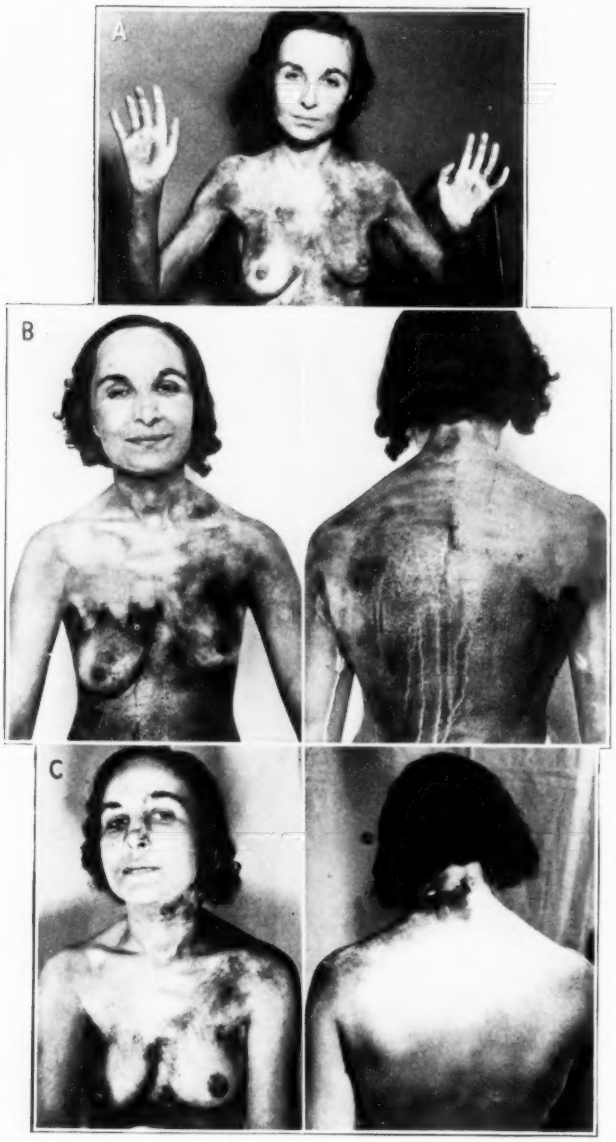


Figure 7

(See legend on opposite page)

while the neural end plate remains chemically stimulable. This explanation is suggested particularly by the fact that after hypodermic injection of pilocarpine the sweating may appear first over the sympathectomized zone. We have witnessed this repeatedly in cases of unilateral preganglionic sympathectomy of the face.

The confusion and inconsistent results which have obtained with respect to pilocarpine sweating are due no doubt to the belief that two weeks is sufficient time for a severed postganglionic fiber to degenerate. While this is true for the nerve fiber, it may not be true for the end plate. We can only assume at present that the point of pilocarpine activity on the sweat gland is the end plate and that a longer time is required for this hypothetic (?) structure to become inactive. We do not question the probability that pilocarpine may stimulate the gland directly in strong concentrations, as for example, when it is injected directly in the gland-bearing area, though we have not studied this phase of the problem ourselves. We have used ⅕ grain of pilocarpine hydrochloride hypodermically in all of our cases. This is the maximum feasible dose, and the concentration which ultimately reaches the skin evidently has no influence on the naked sweat gland.

We believe that the pilocarpine anhidrosis is not due to disuse and atrophy of the gland or to vasomotor changes incident to sympathectomy.

EXPLANATION OF FIGURE 7

Fig. 7 (L. C., case 7).—*A*, thermoregulatory sweating forty-six days after a section of the anterior and posterior roots from the first to the fifth thoracic segment, inclusive, bilaterally. There are anhidrosis of the face and some hyphidrosis over the chest.

B, thermoregulatory sweating test fourteen months after the operation described under *A* and four months after removal of the inferior cervical and first dorsal sympathetic ganglia on the right. The front view shows anhidrosis of the face. On the left there is hyphidrosis of the neck and shoulder. On this occasion the result on the left corresponded closely with that shown in *A*. There is anhidrosis on the right in the distribution of the removed ganglia. The rear view reveals good sweating on the left side of the neck and anhidrosis on the right in the distribution of the removed ganglia.

C, pilocarpine sweating test fourteen months after the rhizotomy and three and a half months after the right ganglionectomy. In the front view there is evidence of sweating on the left side of the forehead (hairline), the left eyebrow and the left side of the nose. (These areas were anhidrotic in the thermoregulatory sweating test shown in *A* and *B*.) The area of cutaneous distribution of the removed ganglia on the right is anhidrotic. If the front views in *B* and *C* (thermoregulatory and pilocarpine sweating, respectively) are compared, it may be seen that the pattern of the lower margin of the anhidrotic zone on the right side of the chest is the same in the two cases. In the rear view there is anhidrosis over the cutaneous zone corresponding to the removed ganglia on the right.

We have obtained easily what we have termed contact sweating [13] up to a year and a half after postganglionic sympathectomy. By this we mean that when two sympathectomized cutaneous surfaces are placed in contact in a warm atmosphere, the corresponding sweat glands for some reason will secrete, whereas the same surfaces when exposed will remain dry no matter to what degree of heat the body is exposed. It appears that the gland has a purely local property of secreting when covered, and for this reason particularly we feel that the skin in question should always be kept exposed and uncovered when one is performing a sweating test. Again, as in case 6, it can be demonstrated that a preganglionectomized sweat gland will respond actively to pilocarpine for two years after sympathectomy. With the postganglionic neuron intact the gland is less likely to atrophy, but it certainly has been in disuse for a long period. Sympathectomy causes vasodilatation in the skin, and it is hardly likely that such a vasomotor change could be responsible for pilocarpine anhidrosis.

In the cases of List and Peet [3] tests were made nine days to two weeks after cervicodorsal ganglionectomy. We feel that this is too early for the effect of complete degeneration to become apparent and that the sweating actually indicated an intact neural end plate on the sweat gland. We do not feel that there is adequate evidence for the presence of cholinergic fibers (parasympathetic or sympathetic) to the sweat glands or cutaneous vessels over the entire body other than those from the thoracolumbar division. We have given evidence to indicate that cutaneous vasodilator nerves course through anterior roots and the thoracolumbar chain and not through posterior roots.[16] Furthermore, if true efferent vasodilator nerves to the skin resided in posterior roots and in cranial nerves and the reasoning of List and Peet was valid, then why does not severe local or general heat, which produces the greatest vasodilatation, cause sweating in the sympathectomized face?

The sensory nerves in themselves evidently play no role in pilocarpine sweating. In cases 5 and 6 the posterior roots from the first to the fifth thoracic, inclusive, had been severed, as well as the anterior roots. After section of the root of the fifth cranial nerve there has been no diminution in thermoregulatory or pilocarpine sweating in our experience.

With reference to injuries of the cord, we again recognize the effect of removal of central inhibition from the glands. Thus, we should expect those glands the central pathway of which has been disconnected to be a little more responsive to pilocarpine. However, the lower half of the body is normally so lacking in response to pilocarpine that with

16. Hyndman, O. R., and Wolkin, J.: The Autonomic Mechanism of Heat Conservation and Dissipation: I. Effects from Heating the Body; Evidence for Capillary Dilator Nerves in Anterior Roots, Am. Heart J., to be published.

central inhibition removed the test for altered function due to injury to the cord is of little value. That the lower half to two thirds of the body normally responds little to pilocarpine has consistently been our experience. List and Peet [3] have also called attention to this fact. The removal of central inhibition as the cause of an increase in the pilocarpine sweating response may explain the otherwise confusing result in Craig's [11] case. A patient with intramedullary disease of the cervical portion of the cord presented a more profuse pilocarpine response on the left half of the body than on the right. It is our opinion that the autonomic tracts were interrupted on the left and preserved to some extent on the right. A thermoregulatory sweating test would probably have reversed the picture. In any case, were it possible to demonstrate sweating levels resulting from injury of the cord, the cutaneous level would not correspond with the level of the cord lesion. We emphasized this in a previous publication,[13] and the statement holds for all sympathetic cutaneous phenomena—vasomotor, pilomotor and sudomotor. The demonstration of levels may have value provided an accurate account is taken of the overlap in sympathetic distribution. We do not feel that these statements apply to the hyperemic level which Fay [17] has described. His is probably an antidromic posterior root phenomenon and corresponds closely with the sensory level.

That a complete transverse lesion of the cord does not diminish pilocarpine sweating is illustrated by the following case: H. R., a white man of 22, sustained a complete transverse lesion of the cord at the sixth cervical segment, as proved by clinical and postmortem examination. Three days after injury a thermoregulatory sweating test revealed complete anhidrosis over the entire body. (From the time of injury his body had been completely dry.) One-fifth grain of pilocarpine hydrochloride injected hypodermically caused drenching sweat from forehead to toes.

The pilocarpine sweating test carried out as we have indicated should therefore be a valid indicator in differentiating the degree to which a sympathectomy is preganglionic or postganglionic. One should not accept the results as valid, however, until at least two months after operation. This clinical test provides an opportunity for obtaining information concerning the cell stations in the various sympathetic ganglia, an investigation which we are pursuing at present. Normal persons vary in relation to the degree of sweating after receiving pilocarpine, and for this reason it is incumbent that a control test be done preoperatively so that the final conclusions may be more accurately evolved.

---

17. Fay, T.: Vasomotor and Pilomotor Manifestations: Their Localizing Value in Tumors and Lesions of the Spinal Cord; Report of Thirteen Verified Cases, Tr. Am. Neurol. A. **53**:466-506, 1927; Arch. Neurol. & Psychiat. **19**:31-46 (Jan.) 1928.

SUMMARY

There is a difference of opinion concerning the reactivity of the denervated sweat gland to pilocarpine. The belief has been overwhelmingly in favor of the proposition that sweating may be stimulated by pilocarpine after degeneration of postganglionic sympathetic fibers and even that section of postganglionic fibers may increase the sensitivity of the gland to pilocarpine. We have attempted to explain this and other confusing phenomena and have presented the results of studies on 8 cases representing different forms of sympathectomy, including a case of complete transverse lesion of the cervical portion of the cord. We have shown that after postganglionic sympathectomy the area of pilocarpine anhidrosis will agree precisely with that of thermoregulatory anhidrosis if at least two months is allowed to elapse after operation. After preganglionic sympathectomy, pilocarpine will induce copious sweating by peripheral action even two years after operation. We feel, therefore, that the test should be valuable in obtaining information concerning the cell stations in the various sympathetic ganglia.

CONCLUSIONS

1. After preganglionic sympathectomy pilocarpine hydrochloride (1/5 grain given hypodermically) will induce free sweating up to a least two years after operation.

2. After postganglionic sympathectomy the pilocarpine test performed two months or longer after operation will demonstrate an anhidrosis the area of which agrees precisely with that of the thermoregulatory anhidrosis.

3. When two months at least has elapsed after operation, the sweat gland the postganglionic neuron of which has been severed will not respond to pilocarpine hydrochloride in 1/5 grain doses.

SUBLINGUAL ABSORPTION OF PROSTIGMINE BROMIDE

HARRY M. SALZER, M.D.
CINCINNATI

Prostigmine bromide, administered orally in the treatment of myasthenia gravis, was first tried by Everts,[1] and there is no question as to the efficacy of this drug when taken by mouth. Viets and Schwab[2] demonstrated that prostigmine bromide can be administered in enteric-coated tablets without any alteration in its value. They also used the drug in eye drops and powder inhalations, without success, but had good results with the use of prostigmine bromide in suppositories. They advised that only oral and parenteral methods of administration be employed.

While prostigmine bromide is effective about an hour or an hour and a half after it is swallowed, nevertheless, under certain circumstances, this interval may be too great. My experience in the following cases shows that a more prompt response may be obtained by placing the prostigmine bromide tablet under the tongue and allowing it to be absorbed from there.

REPORT OF CASES

CASE 1.—W. T., a minister (referred by Dr. Samuel Herman), noticed stiffness of the right cheek on Sept. 4, 1938, which was followed on September 6 by drooping of the left lid, weakness of the right arm and fatigue in the muscles of the right leg. Two weeks later he had double vision, and six months later difficulty in articulation developed. A diagnosis of myasthenia gravis was made. His symptoms were always relieved by prostigmine bromide.

On Oct. 16, 1939, when he officiated at a funeral service, he did not take prostigmine long enough ahead, and consequently his pronunciation was poor. A few weeks later, at a banquet, he was suddenly informed that he was to speak; again, the drug, taken on a full stomach, was not effective quickly enough to improve his articulation. In fact, he has noticed little effect from prostigmine bromide when swallowed. Since his weight is 215 pounds (97.5 Kg.), 8 or 9 tablets of prostigmine bromide has been a necessary daily dose.

The patient now breaks the tablets in halves or quarters and places them under his tongue, slight improvement being noticed in fifteen minutes and marked improve-

From the May Institute for Medical Research of the Jewish Hospital, and the Department of Internal Medicine, Neurological Division, University of Cincinnati College of Medicine.

1. Everts, W. H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmine, Bull. Neurol. Inst. New York **4**:523-530 (Dec.) 1935.

2. Viets, H. R., and Schwab, R. S.: The Diagnosis and Treatment of Myasthenia Gravis, J. A. M. A. **113**:559-562 (Aug. 12) 1939.

ment in thirty minutes. Although the prostigmine is placed under the tongue, there has been no local effect on the muscles of speech, for the patient has observed that phonation improved last.

When he awakens in the morning, he is barely able to move or swallow. He places 2 prostigmine bromide tablets under his tongue and within half an hour is able to dress, eat breakfast and tend to the furnace.

CASE 2.—L. P., a girl of 14 (referred by Dr. Louis Sommer), who has marked involvement of the pharyngeal muscles, has never taken prostigmine bromide except by placing it under the tongue. She has not found the taste objectionable. She obtains a good response in forty-five minutes.

CASE 3.—F. W., a man of 75 (seen with Dr. Harold Schiro), formerly swallowed 2 prostigmine bromide tablets three times a day. When the drug was taken in this way, the effect did not appear for forty-five minutes and lasted for only one hour. With sublingual administration of prostigmine bromide, he was able to reduce the dose to 1 tablet and the drug was effective in ten minutes, the effect lasting two hours.

Previously, the patient had occasionally taken 2 tablets on an empty stomach, which produced gastric pain so severe that he had to take atropine. Now, on an empty stomach, he takes 1 tablet by the sublingual route and has no increased peristalsis. He is so pleased with this new method of administration that he would no longer consider swallowing the tablets.

It is suggested that in cases with bulbar palsy the sublingual method of administration might be especially helpful, for Viets, Mitchell and Schwab [3] reported a case in which an injection of prostigmine methylsulfate had to be given before the patient could even swallow a tablet.

CONCLUSIONS

As a result of the improved reaction to prostigmine bromide when given by the sublingual method, it has been possible to reduce the daily dose. Undoubtedly more rapid absorption takes place when the tablet is dissolved in the mouth.

When parenteral administration of prostigmine methylsulfate is not available and a more prompt response from the drug is desired, sublingual administration of prostigmine bromide is recommended.

---

3. Viets, H. R.; Mitchell, R. S., and Schwab, R. S.: Oral Administration of Prostigmine in the Treatment of Myasthenia Gravis, J. A. M. A. **109**:1956-1959 (Dec. 11) 1937.

Case Reports

PORENCEPHALIC CYST

Report of a Case with Arteriographic Studies

VICTOR W. EISENSTEIN, M.D.
Resident in Neuropsychiatry, Welfare Hospital for Chronic Diseases
AND
HENRY K. TAYLOR, M.D.
Roentgenologist, Welfare Hospital for Chronic Diseases
NEW YORK

Porencephaly is a lesion of rare occurrence, but it is of considerable clinical and pathologic interest. A true porencephalic cyst is a fluid-filled cavity located in the cerebral or the cerebellar structure and communicating with one of the ventricles. Commonly, the clinical association of convulsions and mental deficiency with spastic paralysis and underdevelopment of one side of the body suggests the presence of this defect. The etiology is diverse, for such cysts may be congenital or acquired, traumatic or inflammatory in origin. While agreement exists that in most instances the porus is the result of an intrauterine inflammatory disease or trauma [1] which interferes with normal cerebral circulation, there are still some doubts as to the exact site of the vascular damage, such as that recently expressed by Patten and associates: [1a] "It cannot be stated with certainty whether the involvement of branches of one of the three major arteries of the brain explains this localized lesion."

The case presented here may shed some light in this connection. Cerebral arteriographic studies were made and correlated with the clinical and encephalographic observations. The study revealed marked involvement of the branches of the middle cerebral artery on the affected (porencephalic) side. The case is of further interest because of the age of the patient. Porencephalic abnormalities usually exist from early childhood and are rarely encountered past the second decade.[1a] In our case the condition, apparently present since birth, was diagnosed in the patient's sixtieth year.

REPORT OF CASE

History.—R. V., a 60 year old single white woman, was admitted to Welfare Hospital for Chronic Diseases July 11, 1939, with the complaint of convulsive seizures since childhood.

The patient was one of six children, none of whom presented any evidence of neurologic disease. She was born spontaneously and developed normally until her

---

From the neurologic service of Dr. E. G. Zabriskie and the Roentgen Ray Department, Welfare Hospital for Chronic Diseases.

1. (*a*) Patten, C. A.; Grant, F. C., and Yaskin, J. C.: Porencephaly: Diagnosis and Treatment, Arch. Neurol. & Psychiat. **37**:108-136 (Jan.) 1937. (*b*) LeCount, E. R., and Semerak, C. B.: Porencephaly, ibid. **14**:365-383 (Sept.) 1925.

fifth year, when she suffered a severe generalized convulsion without loss of consciousness. She was late in starting her schooling because of a "lame left arm and leg." She attended school only to the third grade; she left at about the age of 12 because she could not learn well. During her early childhood she had no serious illnesses, operations or injuries but had considerable difficulty in getting about because of paresis of the left arm and leg. At the age of 13 she began to have convulsions involving the paretic side, usually with loss of consciousness. At first these occurred two to four times weekly, but as she grew older, they lessened in both frequency and severity.

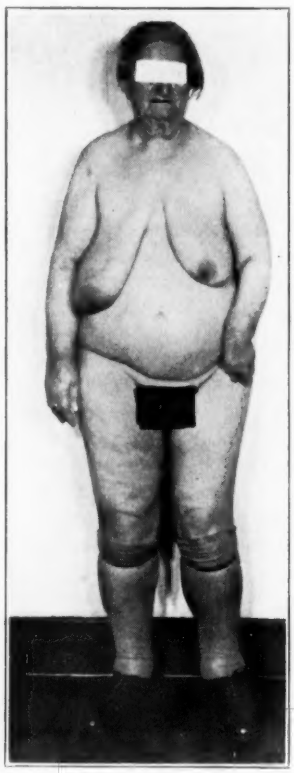


Fig. 1.—Photograph showing the underdevelopment of the left half of the body. Note particularly the size of the left arm and that of the left breast compared with those of the right side.

In adult life she grew obese, but the left side of her body was observed to be less developed than the right. The menstrual history was normal; menopause occurred in her fiftieth year. She never worked or made other than a semi-invalid adjustment, receiving care in various institutions.

Within the ten years prior to admission she had suffered only occasional "epileptic" (usually generalized) attacks during which she lost consciousness and had twice sustained burns by falling on heated objects. It is not known definitely whether there was incontinence during these attacks.

Physical Examination.—The patient, an elderly obese female, was ambulatory but scraped her left foot in walking. Her weight was 205 pounds (93 Kg.); pulse rate, 80 per minute; temperature, normal; blood pressure, 140 systolic and 80 diastolic. The head was small in relation to the body, measuring 51 cm. in circumference. There was general underdevelopment of the left half of the body. The left arm was shorter and much thinner than the right; the right arm had a midbiceps circumference of 38 cm.; the left, one of 31 cm. The left leg was 2 cm. shorter than the right; the midthigh measurements were, right, 58 cm.; left, 50 cm. The left breast was about two thirds the size of the right (fig. 1).

The skin was dry and wrinkled over the entire body, and the features of the face were coarsened. No abnormality was present in the eyes, nose or throat. The thyroid gland was barely palpable. Both carotid arteries were readily palpable and pulsated equally. Percussion revealed that the heart was of normal size; the rate and rhythm were normal, and there were no murmurs. The lungs were clear and resonant. Abdominal and pelvic examinations disclosed no abnormalities.

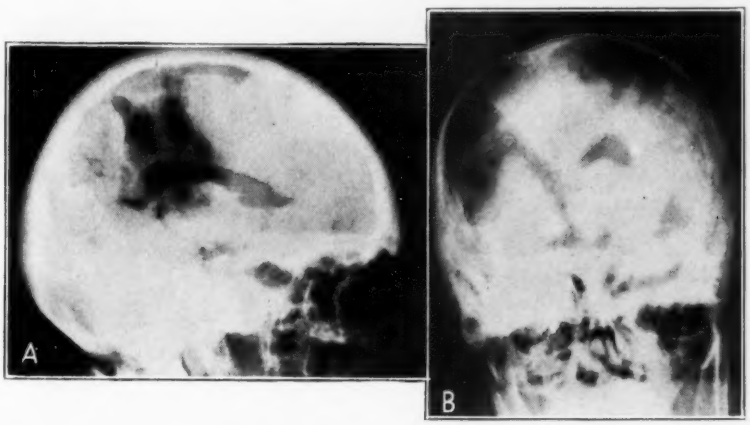


Fig. 2.—*A*, large localized collection of air in the right parietal region (porencephalic cyst). *B*, large porencephalic cyst in the right hemisphere communicating with the ventricle; a collection of air in the subarachnoid space (cortical atrophy) in the left hemisphere.

Neuropsychiatric Examination.—The patient was mentally dull but was on the whole well oriented and attentive. Her memory was poor both for recent and for remote events and for test numbers. She was able to do simple sums. Her mood was generally one of relative apathy, but she was easily irritated by questioning. Tests showed an intelligence of the low moron level (intelligence quotient, 56 per cent).

The cranial nerves were normal. In the right fundus oculi there were changes suggestive of macular degeneration, choroidal pigment deposits and narrowing of the blood vessels. The visual fields could not be adequately tested because of lack of cooperation but appeared normal from gross confrontation tests. Caloric and vestibular tests elicited normal responses.

The gait was spastic, and the left foot scraped in circumduction. The left foot was inverted. Considerable spastic paresis was present in the left upper extremity

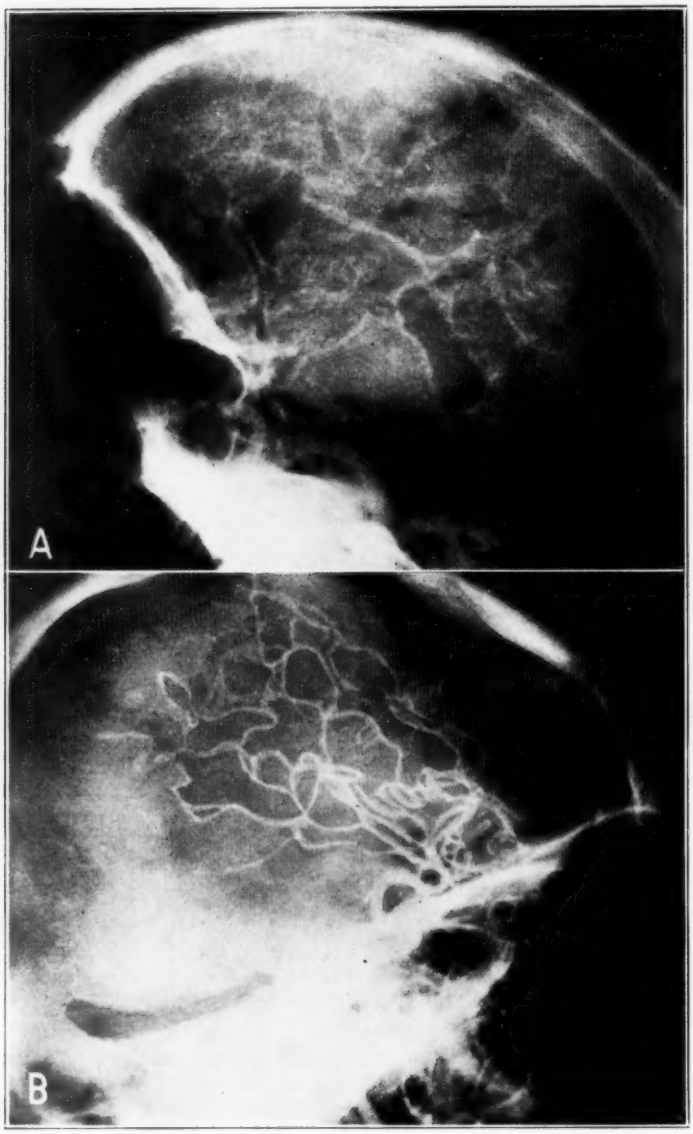


Fig. 3.—*A*, arteriogram of the involved (right) side showing the S-shaped course of the internal carotid artery in the cavernous sinus. The sylvian group of vessels is not visualized. Only the anterior cerebral artery curving over the corpus callosum is shown. *B*, arteriogram of the normal (left) side showing the typical course and distribution of the sylvian group of middle cerebral arteries. The S-shaped course of the internal carotid artery at the base of the skull is well illustrated.

and shoulder girdle, together with flexor contraction at the elbow. The left hand was deformed in extreme flexion at the wrist, and there was hyperextension of the fingers. Synkinetic movements were exaggerated in the left arm. The deep tendon reflexes were hyperactive in both the left extremities. The abdominal reflexes were equal. No Babinski sign was present. No evidence of sensory impairment could be detected.

Laboratory Examinations.—The blood count and urinary findings were normal. Wassermann and Kline blood tests yielded negative results. The spinal fluid was clear, under an initial pressure of 100 mm. of water and contained no cells. The Pandy reaction was negative, and the dynamics were normal. The Wassermann reaction of the spinal fluid was negative; the colloidal gold curve was 0000123331. The basal metabolic rate was —18 per cent. The dextrose tolerance test revealed a high curve with return to normal in two and a half hours.

The roentgenographic examinations of the skull and long bones discovered no abnormalities.

The encephalogram (125 cc. of air injected) showed a large collection of air in the right parietal region, communicating with the lateral ventricle of that side. The findings were characteristic of porencephalic cyst (fig. 2 *A* and *B*). There were also large collections of air in the subarachnoid space, particularly over the left hemisphere, consistent with other evidence of marked cortical atrophy.

Cerebral Arteriography.—Twelve cubic centimeters of a 12.5 per cent solution of colloidal thorium dioxide (thorotrast) was rapidly injected into each carotid artery just below the bifurcation through an 18 gage needle. A lateral projection was made two seconds after the beginning of the rapid injection.

The arteriogram revealed the absence of vessels on the right side of the brain, particularly the sylvian group of middle cerebral arteries (fig. 3 *A*). Only the anterior cerebral artery and its branches were well visualized on the right side. The arteriogram of the left side was normal in appearance (fig. 3 *B*) and showed the course of the middle cerebral vessels streaming off from the S-shaped portion of the internal carotid artery.

COMMENT

This case, like many others reported, revealed a notable disproportion between the cerebral involvement and the clinical symptoms. The porencephalic cyst extended wide and deep about the region of the central sulcus on the right side of the brain, but sensory disturbances were not evident, despite the extension of the lesion into the parietal region. However, underdevelopment of the left breast, arm and leg was striking. Jacksonian attacks on the patient's left side were infrequent, generalized convulsions occurring almost as often. The degree of mental impairment was correlated with the extent of cortical atrophy, as demonstrated by encephalograms, and with the general avascularity of the convexity of the right hemisphere, as demonstrated by arteriograms.

The porus was undoubtedly of congenital origin. Injury at birth and syphilitic or tuberculous infection may be ruled out as causative factors; fetal maldevelopment or intrauterine meningoencephalitic changes appear more likely to have been the causes. Pathologic study [2] has shown that the porencephalic process begins as fetal meningoenceph-

2. Globus, J. H.: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:654-668 (Dec.) 1921.

alitis, which leads to strangulation, endarteritic change or thrombosis of the vessels in the involved area with resultant anemic necrosis and the formation of a cavity in the brain substance. Arteriographic evidence of widespread involvement of the middle cerebral artery is presented in connection with the porencephalic cyst in this case.

SUMMARY

A case of porencephaly is presented with encephalographic and arteriographic studies demonstrating marked involvement of the middle cerebral artery in relation to the cerebral cyst.

News and Comment

THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

At the meeting of the board held at Washington, D. C., May 2 and 3, 1941, the following candidates were granted certificates:

Psychiatry.—By Examination: Leslie P. Adams, New York; Asher L. Baker, Beacon, N. Y.; Ellis Bonnell, Chicago; Edward J. Carroll, Washington, D. C.; Robert Alfred Clark, Howard, R. I.; George H. Cook, Gallipolis, Ohio; Patrick H. Drewry Jr., Richmond, Va.; Eugene I. Falstein, Chicago; Samuel Feinstein, Ogdensburg, N. Y.; Ralph Manos Fellows, Milwaukee; James A. Flaherty, Philadelphia (Wauwatosa, Wis.); E. Philip Freeman, Westboro, Mass.; Daniel Haffron, Elgin, Ill.; Meta F. Haldeman, Washington, D. C.; Werner Hamburger, Utica, N. Y.; George T. Harding, Columbus, Ohio; Herbert E. Harms, Colorado Springs, Colo.; Gert Heilbrunn, Elgin, Ill.; Jay L. Hoffman, Washington, D. C.; Paul M. Howard, Waverley, Mass.; Clara L. Hoye, Washington, D. C.; Jacob R. Jacobson, Elgin, Ill.; Paul Lemkau, Baltimore; Theodore F. Lindberg, Dorchester Center, Mass.; Martha W. MacDonald, New Orleans; Harry H. Michelson, Northampton, Mass. (New Orleans); William F. Murphy, Scituate, Mass.; Lincoln Rahman, New York; Seymour J. Rosenberg, Camp Lee, Va.; Morris L. Sharp, Foxboro, Mass.; W. Leland Sharp, Anderson, Ind.; David Slight, Chicago; Bruno Solby, New York; Hamlin A. Starks, Orangeburg, N. Y.; D. Louis Steinberg, Elgin, Ill.; Sidney Tarachow, New York; Charles V. Taylor, Cambridge, Md.; Morton L. Wadsworth, Farnhurst, Del.; Samuel R. Warson, Louisville, Ky.; John H. Waterman, Harrisburg, Pa.; Harry I. Weinstock, New York; Helen Yarnell, New York; Frederick T. Zimmerman, New York.

On Record: Paul S. Johnson, Richmond, Ind.; Henry A. Luce, Detroit; Cleophas E. Poellot, Woodville, Pa.; Theophile Raphael, Ann Arbor, Mich.; Frederick H. Weber, Worthington, Ohio; Mary J. Weber, Worthington, Ohio; Frank L. Whelpley, Goldsboro, N. C.; Mary Wickens, Richmond, Ind.

Neurology.—By Examination: Francis C. Ansanelli, New York; Rudolf J. Baruch, Elizabeth, N. J.; W. de Gutierrez-Mahoney, Nashville, Tenn.; Ralph L. Drake, Wichita, Kan.; * Calvin S. Drayer, Upper Darby, Pa.; Harrison Evans, Columbus, Ohio; Lawrence C. Kolb, Baltimore; * Zigmond M. Lebensohn, Washington, D. C.; Lewis H. Loeser, Newark, N. J.; * George N. Raines, Philadelphia.

On Record: * Serge Androp, Catonsville, Md.; Benjamin Pushkin, Baltimore.

Neurology and Psychiatry.—By Examination: Alex Blumstein, Minneapolis; Meyer Brown, Chicago; John M. Caldwell, Washington, D. C.; G. Colket Caner, Boston; Mandel E. Cohen, Washington, D. C.; Isidore Finkelman, Chicago; Leon Freedom, Baltimore; Alfred Gallinek, New York; Jacques S. Gottlieb, Iowa City; G. Edgar Hobbs, Boston; Ben W. Lichtenstein, Chicago; Lillian McGowan, New York; Sam Parker, Brooklyn; Milton Rosenbaum, Cincinnati; Elvin V. Semrad, Waltham, Mass.; Lewis I. Sharp, New York; Eugene L. Sielke, Philadelphia; Stephen Weisz, Galveston, Texas; Ernest Y. Williams, Washington, D. C.

On Record: Siegfried Baumoel, Cleveland; N. Lionel Blitzsten, Chicago; William J. Dougherty, Yonkers, N. Y.; Emanuel D. Friedman, New York; Forrest

* This award is complementary to one previously granted in psychiatry.

M. Harrison, Washington, D. C.; Louis Hausman, New York; Otto Lowenstein, New York; Garland H. Pace, Provo, Utah; William Clare Porter, Washington, D. C.; Edward A. Steinhilber, Philadelphia; Lewis D. Stevenson, New York; Michael Vinciguerra, Elizabeth, N. J.

THE MILITARY MOBILIZATION COMMITTEE OF THE AMERICAN PSYCHIATRIC ASSOCIATION

The Military Mobilization Committee of the American Psychiatric Association has assembled through its subcommittee dealing with civilian mental health a considerable amount of information concerning behavior reactions which have appeared in other countries, particularly those which are actively belligerent. This information, together with data concerning the measures which have been taken to deal with these reactions, has been compiled in reports which are available to the members of the association. These reports can be obtained on application to Dr. D. Ewen Cameron, Albany Hospital, Albany, N. Y.

INTERNATIONAL LEAGUE AGAINST EPILEPSY

At a meeting in Richmond, Va., on May 5, the American branch of the International League Against Epilepsy elected the following officers for the ensuing year: president, Dr. H. Houston Merritt, of Boston; vice presidents, Dr. David C. Wilson, of University, Va., and Dr. Milton Rosenbaum, of Cincinnati; secretary-treasurer, Dr. F. A. Gibbs, of Boston; vice president for America of the International League, Dr. Adolf Meyer, of Baltimore.

Abstracts from Current Literature

Physiology and Biochemistry

THE EFFECTS OF PHENOBARBITAL ON MUSCULAR STEADINESS. ARNOLD P. FRIEDMAN, Bull. Los Angeles Neurol. Soc. **5**:120 (June) 1940.

Friedman used a "Whipple steadiness tester," which measures the ability of the subject to hold a metal stylus suspended in a hole without touching the sides, to determine the effect of 1.5 grains (0.975 Gm.) of phenobarbital on the function of "steadiness." Subjects taking phenobarbital showed a slight decrease in steadiness when tested for three hour periods. Although the tremor tested was of the intention type, Friedman suggested that the use of phenobarbital might increase the rest tremor of parkinsonism.

MACKAY, Chicago.

CREATINE-CREATININE METABOLISM AND THE HORMONES. H. H. BEARD and E. J. JACOB, Endocrinology **26**:1064 (June) 1940.

Beard and Jacob report the results of parenteral injections of creatine or creatinine, with and without androgen and estrogen, into normal rats. The injection of creatine in doses of from 25 to 200 mg. does not increase the excretion of creatinine but causes its retention. The injection of similar amounts of creatine together with androgen and estrogen causes an increase in the excretion of creatine but not in that of creatinine. The injection of either androgen or estrogen alone likewise fails to produce an increase in the excretion of creatinine, but does cause an increase in the excretion of creatine.

From these results the authors conclude that (*a*) creatine is not changed into creatinine in the rat; (*b*) androgen and estrogen do not assist in the creatine-creatinine transformation or in creatinine excretion; (*c*) under proper experimental conditions the injection of creatinine stimulates the excretion of creatine and the injection of androgen or estrogen increases this function of creatinine, and (*d*) no difference in the effect of androgen or of estrogen on creatine-creatinine metabolism in rats has been noted.

PALMER, Philadelphia.

CREATINE-CREATININE METABOLISM AND THE HORMONES. H. H. BEARD and E. J. JACOB, Endocrinology **26**:1069 (June) 1940.

Beard and Jacob report the effects on the creatine and creatinine excretion in the urine of parenteral injections of androgen and estrogen (testosterone propionate and estrone [theelin]), with and without saline solution and creatinine, into male and female rats castrated ninety days previously. In these older castrated animals the injection of the androgen or estrogen did not cause an increase in creatine excretion above that obtained by the injection of saline solution alone, which is in contrast to the increase in creatine excreted by the normal or by the recently castrated animals under similar experimental conditions.

The authors present a brief summary of pertinent observations discussed in the three previous papers on this subject. (*a*) In the normal rat injection of androgen and estrogen (testosterone propionate, estrone [theelin], progestin and anterior pituitary extracts containing the growth and thyrotropic principles) causes creatinuria, which is not due to creatinine but is the result possibly of water and salt retention. (*b*) In the normal rat injection of creatinine causes creatinuria, as a result of the hydrolysis of creatinine to creatine and the stimulating effect of creatinine on creatine excretion. (*c*) In the normal rat injection of androgen and estrogen plus creatine produces creatinuria; the stimulating effect of creatinine on creatine excretion is increased in the presence of either androgen or estrogen.

(*d*) Recent castrates show temporary creatinuria, some of which is due to the anesthetic and the trauma of the operation. (*e*) In recent castrates injection of androgen and estrogen (estrone, testosterone propionate and progestin, as well as anterior pituitary extracts containing the growth and thyrotropic principles) causes creatinuria, which is more intense in the castrated animal than in the same animal before castration. (*f*) In three and six month castrates injections of androgen and estrogen plus creatinine causes creatinuria, which is due to the injection of saline solution alone. (*g*) In normal, recently and old castrated animals injection of saline solution causes creatinuria, which is due to the hydrolysis of creatinine to creatine.

PALMER, Philadelphia.

THE DEPOSITION OF LIPIDS IN VARIOUS PARTS OF THE CENTRAL NERVOUS SYSTEM OF THE DEVELOPING RAT. B. A. FRIES, C. ENTENMAN, G. W. CHANGUS and I. L. CHAIKOFF, J. Biol. Chem. **137**:303, 1941.

The deposition of cholesterol, phospholipid and total fatty acids was studied in various divisions of the central nervous system (spinal cord, medulla, cerebellum and forebrain) of the rat from birth until the animal attained a weight of 300 Gm. In each part of the central nervous system the maximum rate of deposition of these lipid constituents occurred during the period between birth and the time the rat attained a weight of 50 Gm. Differences in lipid composition were found in all parts of the central nervous system. Throughout the entire period of observation, the spinal cord contained the highest amounts of cholesterol, phospholipid and total fatty acids. The medulla was next in order. The lipid composition of the cerebellum and that of the forebrain were almost identical at all periods in which they were studied, and the lipid content of the two regions was always lower than that in either the spinal cord or the medulla. The pattern with respect to the amounts of cholesterol, phospholipid and total fatty acids contained in each division of the central nervous system from birth until full growth is maintained relatively constant.

PAGE, Indianapolis.

A STUDY OF CHOLESTEROL ESTERASE IN LIVER AND BRAIN. W. M. SPERRY and F. C. BRAND, J. Biol. Chem. **137**:377, 1941.

Sperry and Brand found that hydrolysis of cholesterol esters does not occur when emulsions of rat brain are incubated with blood serum. Liver, on the other hand, esterifies cholesterol actively over a wide p_H range. The factor in liver is different from the esterifying enzyme in blood serum.

PAGE, Indianapolis.

THE ELECTRO-ENCEPHALO-CARDIOGRAM. DANIEL E. SCHNEIDER and CLARENCE C. CLARK, J. Nerv. & Ment. Dis. **91**:742 (June) 1940.

By placing one lead over the occiput and the other over the spine of the seventh cervical vertebra, Schneider and Clark obtained a single tracing of the combined changes in electric potential occurring in the cerebral cortex and in the heart. They were thus able to determine the temporal relations between the alpha and beta waves and the QRS complex. In the normal adult five to six alpha waves and twenty-five to fifty beta waves occurred to one QRS complex. Since cortical wave frequency increases with age, up to 12 years, and the heart rate decreases, the ratio of alpha and beta waves to the QRS complex is constantly increasing during that time. Schneider and Clark believe that the ability simultaneously to measure cerebral and cardiac potentials provides a basis for experiments in "integrative physiology."

MACKAY, Chicago.

RAISED INTRACRANIAL PRESSURE: HYDROCEPHALIC AND VASCULAR FACTORS. HUGH CAIRNS, Brit. J. Surg. **27**:275 (Oct.) 1939.

Contrary to much belief and teaching, a tumor or other mass in one part of the brain may increase the intracranial pressure locally and not disturb it generally,

the limiting falx, the tentorium cerebelli and the irregular shape of the base of the skull being responsible for this condition. Consequently, decompressions to relieve localized pressure are frequently inadequate and may be dangerous rather than helpful. Decompression to produce its greatest effect should immediately overlie the tumor.

Relief of pressure at operation is of primary importance in the removal of tumors of the brain. Most surgeons welcome the welling up of cerebrospinal fluid from the depths of a wound because it is evidence that the obstruction brought about by the tumor has been relieved.

Aside from that due to an intracranial mass, increase in intracranial pressure is the result of venous congestion more often than of arterial hypertension. Cairns describes the effect of carbon dioxide inhalation on the elevation of intracranial pressure. From a normal pressure of approximately 100 mm. of water, administration of 1 per cent carbon dioxide for three minutes produced a rise in spinal fluid pressure to 125 mm.; administration of 2.5 per cent carbon dioxide for two minutes resulted in a spinal fluid pressure of 180 mm., and administration of 5 per cent carbon dioxide for two minutes resulted in a spinal fluid pressure of 320 mm.

Cairns cites several cases in which the brain obviously began to swell at operation as a result of the administration of carbon dioxide. In 1 case hemorrhage occurred into a tumor and death resulted; in another severe edema and engorgment of cerebral veins around a tumor took place.

STUCK, Denver.

THE EFFECT OF RAISED INTRACRANIAL PRESSURE ON THE CEREBRAL BLOOD FLOW. F. C. COURTICE, J. Neurol. & Psychiat. **3**:293 (Oct.) 1940.

Courtice studied the effect of increased intracranial pressure on the cerebral blood flow (*a*) in unanesthetized human subjects suffering from intracranial tumor and (*b*) in anesthetized cats in which artificial tumors had been inserted extradurally either in the frontal or in the cerebellar region. The blood flow was measured by the arteriovenous differences in the oxygen and carbon dioxide contents of the blood and by the percentage saturation of the hemoglobin with oxygen under conditions of rest, when the rate of the metabolism of the brain is assumed to be constant. The author found that of the 23 human subjects, those with tumors in the frontal or parietal region gave results which were approximately normal, while those with tumors in the posterior fossa or the basal ganglia showed an increased arteriovenous difference and a lower percentage saturation of the venous blood with oxygen; that is, the cerebral circulation was definitely slower than normal. Similar results were obtained in the experiments on cats, in which only the group with cerebellar tumors showed a slower blood flow. Hydrocephalus was associated only with the tumors of the posterior fossa both in the human subjects and in the cats. The coefficient of oxygen utilization corroborated these findings, and it was estimated that the cerebral blood flow was approximately 30 per cent less in the cases of tumors of the cerebellum or basal ganglia than in those of tumors of the frontoparietal region. In 5 human subjects surgical removal of the tumor reduced the arteriovenous oxygen difference to normal only when this was previously high. When a sudden rise in intracranial pressure was produced by mechanical pressure on a bony defect in human subjects who previously had a decompression, it was observed that the blood flow was not affected if the pressure was raised in the temporoparietal regions but that it was frequently slowed if pressure was exerted posteriorly at the base of the skull. This difference observed in the two groups of subjects is explained by the local pressure effects of the tumor. Thus, a tumor at the base of the brain has a greater influence on the large venous channels as they converge toward the base of the skull than a tumor in the frontoparietal cortex. In the latter instance local changes in the circulation probably also occur, but they do not produce any appreciable effect on the general cerebral circulation.

MALAMUD, Ann Arbor, Mich.

Psychiatry and Psychopathology

THE PROBLEM OF SYPHILITIC PSYCHOSIS. ERWIN WEXBERG, Am. J. Syph., Gonor. & Ven. Dis. **24**:590 (Sept.) 1940.

Parenchymatous and interstitial syphilis of the central nervous system are distinguished as pathologic entities. There is, however, at times distinct overlapping of the processes, which has been recognized by pathologists but neglected clinically. Palsies of the ocular muscles, for example, occur so frequently in the early stage of tabes dorsalis that they are thought to be part of the clinical picture, whereas they are really due to basal syphilitic meningitis.

There is considerable uncertainty in the differential diagnosis of dementia paralytica, and not every case of organic psychosis in a syphilitic patient can be so classified. The essential consideration is to make a distinction between dementia paralytica and syphilitic psychosis. A review of the literature reveals but scant consideration of this differentiation.

Wexberg analyzed 256 cases of cerebrospinal syphilis, among which there were 38 cases of dementia paralytica, 6 of cerebral syphilis with psychosis and 20 in which a differential diagnosis between dementia paralytica and cerebral syphilis was impossible with the clinical methods available. The psychiatric manifestations of the patients who did not have dementia paralytica may be divided into seven types, which show considerable overlapping: hallucinosis without confusion; confused states with or without paranoid delusions and hallucinations; states of clouded sensorium; dementia; epileptic psychosis; manic-depressive states, and schizoid reactions.

A definite differential diagnosis between syphilitic psychosis and dementia paralytica could not be made in 20 cases. The author presents the following criteria for not considering them cases of the latter disease:

(1) Early appearance of marked neurologic symptoms other than those characteristic of tabes. In cases of dementia paralytica they are usually terminal. (2) Presence of psychiatric syndromes which are uncommon in dementia paralytica, such as hallucinosis, stuporous and delirious states and schizoid and organic reaction types. (3) The patient's age and state of disease. Dementia paralytica is predominantly a disease of middle life; therefore persons in their late twenties are too old for the juvenile form of the disease and too young for the acquired form, since the period of incubation ranges from eight to twenty years. (4) Cure with ordinary antisyphilitic therapy. In instances in which this is obtained the psychosis is less likely to be dementia paralytica. (5) Spinal fluid findings. A negative Wassermann reaction of the spinal fluid is rare in cases of dementia paralytica. The cell count and the protein and colloidal gold reactions are more markedly positive in dementia paralytica than in other forms of neurosyphilis, but according to the author they are not crucial.

Every patient with a psychotic reaction and a positive Wassermann reaction of the spinal fluid, if there are no specific contraindications, should be submitted to radical therapy for dementia paralytica, even though some patients will be included who might have improved under milder therapy.

BECK, Buffalo.

TYPES AND ANALYSES OF THE CLINICAL PICTURES OF RECOVERED SCHIZOPHRENICS. OTTO KANT, Psychiatric Quart. **14**:676 (Oct.) 1940.

Kant made a follow-up study of 39 patients whose disease was diagnosed as schizophrenia during hospitalization and who four years or more after discharge were found to be recovered. Only exemplary material was presented. The author found that in most of the cases in which the patient recovered there was a psychogenic aspect, a definite precipitating conflict with reality, with concentration of the psychotic content about this conflict and the reality experiences. The clinical pictures were classified according to the following general characteristics: Group 1: (*a*) Gradual depression with shallow affect and tendencies to stupor: (*b*) acute onset of persecutory ideas with marked anxiety and self depreciation.

Group 2: Depression followed by excitement (despite shallow affect) with grandiose, religious delusions and hallucinations. Group 3: Alternation of pictures presented by groups 1 and 2. Group 4: Excitement and stupor states with incoherence and destructivity. Group 5: More classic schizophrenic features, such as catatonia and paranoid psychoses.

On the basis of the affective changes, the author believes that disturbances falling in the first three groups should not be classified as schizophrenia. The fourth group was felt to be dominated by neither affective nor schizophrenic symptoms. The last group most nearly resembled typical schizophrenia in its psychopathologic features but still showed the relations to reality conflicts which characterized the entire series. SIMON, Worcester, Mass.

INTROJECTION, PROJECTION AND IDENTIFICATION. ROBERT P. KNIGHT, Psychoanalyt. Quart. **9**:334, 1940.

Knight points out that there is some confusion in analytic literature about the meaning of introjection, projection and identification. He defines introjection as equivalent to incorporation and as the unconscious inclusion of the object or part of the object in the ego. It is an id process, which alters the structure of the ego of the subject and involves a previous projection of the subject's own unconscious tendencies. Projection is the mechanism by which the subject attributes his own unacceptable unconscious tendencies to an object and perceives them as tendencies possessed by the object. It is an unconscious ego or superego process for dealing with id tendencies and results in the alteration of the perceived character of an outside object. Identification is not a mechanism and is not synonymous with introjection, but is an accomplished fact. It may result from several different mechanisms acting separately or together: 1. If a subject admires an object and wishes to be like him, he identifies himself with the object by introjection. 2. If a subject puts himself in the place of the object and feels that in a given situation the object would react as the subject would, the subject's ideals of behavior are not affected but his feelings are projected onto the object. This is commonly seen in the condition known as altruistic surrender. The subject, because of a sense of guilt, denies himself his desired gratifications and projects his "guilty" desires onto the object so that the object's pleasure becomes his pleasure. This process circumvents the subject's superego and enables the subject to repress all envy. Intuition is a special form of this mechanism; that is, it is the capacity for an accurate selective projection of one's own needs and feelings onto another person. 3. The subject identifies an object B with an object C. This occurs through the use of the mechanisms of displacement and substitution, with the use also of projection and introjection.

In most instances identification is the result of a complete interaction of the mechanisms of projection and introjection.

Knight points out that falling in love involves an interaction of projection and introjection. He also notes that normal persons under certain circumstances experience a feeling of depression similar to that in melancholia. This happens because the normal self regard is determined by (1) a more or less objective evaluation of the self; (2) a more or less illusional evaluation of the self and (3) a partly objective and a partly illusional evaluation of the self based on one's ideas of what one's friends think of one, i. e., a projected partly valid, partly illusional evaluation of the self. This projected self love gives the object the characteristic of the self, and if the subject is rebuffed he feels that this projected self love is in danger of being lost and reacts to this threat of loss by depression. PEARSON, Philadelphia.

ON MISIDENTIFICATION. T. KASANIN, Psychoanalyt. Quart. **9**:342, 1940.

Misidentification is a symptom commonly occurring in psychoses and in toxic states, although it occurs also in the psychoneuroses. Kasanin reports a case in which misidentification was the solitary mechanism whereby the patient was able to

relieve herself of depression. The patient was an elderly woman who became depressed after the disappearance of her beloved only son, who was never heard of again. While in the hospital, the patient mistook an intern for her son—there was some slight resemblance. After a period her depression was relieved. Depression is the means by which a person attempts to overcome the feeling of loss of a love object; that is, it is caused by the persons's attempts to eject the introjected love object. Usually this is accomplished by replacing the lost love object with another love object, but if there is lack of capacity or possibility of such replacement or if the identification of the ego and the love object is too great other ways must be found. In the case cited the patient was able to overcome her feeling of loss by perceiving the intern as her lost son and then gradually separating herself from him. Thus, through small doses she was able to overcome her mourning, just as allergic sensitivity is overcome by small doses of the allergic substance. Misidentification therefore is a method by which a person can displace an introjected love object to one whose loss will be less painful.

PEARSON, Philadelphia.

THE DYNAMICS OF THE DISSOLUTION OF TRANSFERENCE RESISTANCE. RICHARD STERBA, Psychoanalyt. Quart. **9**:363, 1940.

Sterba points out the importance for cure by analysis of the dissolution of the transference resistance. Transference resistance occurs when the patient transfers onto the analyst feelings of love, hate or fear which enable him to avoid producing further material from his unconscious. He cites the case of a passive, submissive man who tried to avoid mentioning unfavorable ideas about the analyst, of whom he became afraid. This fear of the analyst hindered bringing into the consciousness one of the patient's most powerful psychic emotions, i. e., his hatred of his father. The fear of the analyst resulted from the attempt of the patient's ego not to discover his hostile wish to castrate the father. The analyst's task, therefore, is to overcome this transference resistance by interpretation. When the analyst interprets the transference resistance he helps the patient to oppose his ego to the instinctual activity released in the transference. He assists the patient's ego by offering an identification which satisfies the reality-testing needs.

By interpretation the analyst endeavors to separate those parts of the ego which face and assess reality from the parts which function in carrying out unconscious instinctual wishes or work to suppress these wishes; that is, he keeps the reality-testing part of the ego from being flooded by material reenacted from the past.

In the case cited, through repeated interpretations of the transference resistance, the patient remembered his fear and hatred of his father. The patient's progress from the development of anxiety to the acted-out manifestations of hatred and the active castration wishes corresponded to a dissolution of the anxiety. This was accomplished by two factors: 1. Through the interpretation of the anxiety in the transference situation the patient's ego was strengthened and was able to recognize the difference betwen reality and infantile fantasy. 2. The absence of an affective reaction on the part of the analyst enabled the patient to recognize that some of his anxiety was irrational.

The interpretations must be made repeatedly because the resistances have been formed over a long period. The dissolution of the transference resistance means the dissolution of resistance resulting from genuine infantile castration anxiety. This liberates supporting resistances, which can then easily be analyzed later.

PEARSON, Philadelphia.

THE STRUCTURE OF THE EGO. ISADOR CORIAT, Psychoanalyt. Quart. **9**:380, 1940.

The ego is a perceptive apparatus for maintaining contact with reality and an instrument for regulating instincts. Dominance of the ego in personality produces a realist, of the superego an obsessive and conscience-ridden person and of the id a person controlled only by his irresistible instinctual desires. The ego is the most prominent part of the personality. It is changeable, and this mutability and

modifiability are dependent on cortical pathways the boundaries of which fluctuate. It is derived from the bodily sensations and is a mental projection of the surfaces of the body and of the superficies of the mental apparatus. One surface of the ego is turned toward the instincts and the other toward sensory perceptions and external reality. If the plasticity of the ego is diminished or lost the functions of the ego are impaired. The synthetic function of the ego depends on the intercortical pathways, and it is these intercortical systems which constitute the apparatus of the consciousness.

In the newborn child the function of the ego consists of an attempt to attain a state of satisfaction by wishing away or ignoring reality. As the child grows the ego becomes an organ for testing reality. The ego is developed from the id and therefore consists of three parts: (1) a conscious part, formed from the perceptive system; (2) a preconscious part, formed from elements just outside the boundaries of ego perception, and (3) an unconscious part, consisting of elements deposited from perceptions. The superego is different, being formed by the introjection of specific experiences related to the oedipus situation.

The ego is exposed to three potential sources of danger: the external world, the id and the superego. The ego learns of a danger through a feeling of anxiety and reacts to this feeling by flight or other protective measures.

In analysis the ego is modified through the process of free association. If the ego is weak, there will be great anxiety and the ego will defend itself by the use of aggression.

Coriat thinks that the hypothalamic drives are synonymous with the demands of the id.

PEARSON, Philadelphia.

INSTINCT DUALISM IN DREAMS. LUDWIG JEKELS and EDMUND BERGLER, Psychoanalyt. Quart. **9**:394, 1940.

Jekels and Bergler state that many analysts do not believe that Freud's division of instincts into Eros and *Todestrieb* is valid. They attempt to show that there is clinical evidence of the dualism of instincts in the phenomena of sleep and dreams. They believe that sleep itself is a manifestation of this dualism. Eros unites with the drive of *Todestrieb* for rest and so transforms the death drive into the recuperative effect of sleep; that is, sleep is "a little death." They believe that dreams have two functions: 1. They keep the dreamer asleep; i. e., they follow the death drive toward absolute rest. 2. They keep the dreamer alive; i. e., because dreams are wish fulfilling and because these wishes are sexual, the dreamer does not sink into absolute rest but follows the path of the erotic instinct.

The authors theorize that dreamless sleep is impossible because the dreamer would die. They state that the ego ideal is formed in part through an attempt of the ego to direct the aggressive impulses away from itself to other objects. These objects would become terrifying if the erotic instinct did not neutralize them by incorporating the fearsome objects into the ego where they become the object of the person's narcissism. In part the ego ideal is formed as a result of a compromise attempt of the ego to maintain its supposed omnipotence. Either the child must give up its fictitious feeling of omnipotence in the face of reality, or it can accept the parental demands by pretending that the compulsory act was voluntary; that is, it clothes the introjected object with its own narcissism. If the erotic instinct were successful in the defense against the death instinct through the formation of the ego ideal by means of identification, the ego ideal would be the abode of love.

Todestrieb parries this move of the erotic instinct by desexualization during the identification. This desexualization means that there is released undifferentiated narcissistic energy, which can unite with either of the two basic instincts. This undifferentiated energy in the ego ideal becomes the prize for which Eros and Thanatos strive. Eros attempts to direct it onto external objects by projection, but this projection is unsuccessful because (1) the infant is helpless and cannot handle large amounts of aggression and (2) the objects of the aggression—the parents—are already in the ego ideal.

These two difficulties lead to a damming up of aggression and a backflow against the ego. The ego becomes frightened and gives the danger signal. Thus the ego ideal becomes pressed into the service of the ego-destroying tendencies. As the presence of the ego ideal makes itself felt in dreams, the authors point out that the freudian concept of the dream as the fulfilment of a wish usually considers the erotic wishes but that in every dream there are two wishes: (1) that emanating from the id and (2) a wish defense against a reproach from the superego, which is detoured through the ego ideal.

The authors use Freud's dream of Irma's injection as an illustration. This dream consists of a complicated series of refutations against the aspersions of inadequate professional conscientiousness which Freud's ego ideal was casting on him because he had learned the day before that Irma was better but not entirely well. Besides this, the dream contains a number of repressed erotic wishes.

Dreams range from those which contain a large number of repressed erotic wishes and aggressive wishes against the ego ideal (a trend toward the erotic instincts) to the anxiety and punishment dreams which show the main trend to the thanatotic instinct.

Every dream has the second component of refutation of superego reproaches and is therefore a compromise formation and a type of fusion of Eros and *Todestrieb*.

PEARSON, Philadelphia.

PSYCHIATRIC COMPLICATIONS OF HYPOGLYCEMIA IN CHILDREN. E. W. ANDERSON, Lancet **2**:329 (Sept. 14) 1940.

Anderson points out that hypoglycemia, whether from overdose of insulin or from hyperplasia or neoplasm of the islets of Langerhans, or from any other cause, shows itself chiefly in symptoms referable to the nervous system. Baker, in 1939, described a prodromal stage of nervousness, sweating, pallor, tremor, sleepiness and salivation, which may pass on to diplopia, muscular twitchings of the face and limbs, hemiplegia and jacksonian or epileptiform attacks. Other disturbances include aphasia, disorders of sensation, hemianopia or complete blindness, auditory changes and incoordination. Finally the patient may become stuporous, with various reflex changes. Psychic disturbances, sometimes accompanying the neurologic signs, may begin as fears, anxieties, mild depression and faulty concentration and pass on to a stage in which the speech is thick, the patient grimaces, laughs or cries without reason and is dull or garrulous, and fugues and hallucinations may result. He may finally lose consciousness and, when he recovers, have no memory of the attack. Other authors describe a wide range of disturbances, including a fall of tension in the eyeballs, akinesia and masklike stiffness of the face, hypothermia, migraine, irritability, megaphony, behavior disorders, such as stealing, personality changes, with euphoric indifference and docility, mild depression, severe agitation and catatonia with grandiose delusions, as well as psychoneurotic pictures. The association of epileptiform convulsions with hypoglycemia, especially in children, has often been noted, but the available evidence shows that the relation between them is not constant. The author reports the histories of 2 children with hypoglycemia in whom neuropsychiatric symptoms developed. In the first child the hypoglycemic coma, which developed after an excessive dose of insulin, lasted four days, and the patient then showed gross generalized dementia with symptoms suggesting an extensive lesion of the left side of the brain. After fifteen months there was only partial recovery of function. The second patient was a diabetic boy who had always been sensitive to insulin. He showed a behavior disorder, which was most manifest when the blood sugar was low. While in a hypoglycemic phase he stabbed another child. After treatment he improved considerably in both intelligence and behavior. The author discusses the difficulties encountered in the treatment of diabetic children and calls attention to the possible dangers from the newer forms of insulin.

J. A. M. A.

BROMIDE INTOXICATION. MERRILL MOORE, THEODORE SOHLER and LEO ALEXANDER, Confinia neurol. **3**:1, 1940.

Moore, Sohler and Alexander review the findings in 100 cases of bromism that have been reported since 1927 and arrive at the following conclusions: Bromide intoxication is occurring with increasing frequency among patients admitted to psychopathic hospitals, largely as a result of inadequate knowledge of the action of the drug. In a great number of cases the toxic manifestations occur as the result of either excessive dosage or cumulative effects due to prolonged use without regular control determinations of the bromide level in the blood. Bromide intoxication is seen most frequently in persons between 40 and 60 years of age, and 64 per cent of the cases occur in women. General social problems, as well as the appearance of increasing organic cerebral changes in this period of life, are underlying factors.

Of 100 cases of bromide intoxication, the bromides had been taken by medical prescription in 63 per cent and were self administered in 22 per cent; in 15 per cent no adequate information could be obtained. Suicidal attempts with bromides are rare. In most instances there is an underlying condition necessitating the use of bromides, and in most cases psychotherapeutic measures can replace the prescription of bromides. Epileptic patients seem to possess a greater tolerance to the drug than do other persons. In a number of cases there seems to be a special idiosyncrasy for the drug. Habit formation does not play an important role.

The most common psychotic manifestation of bromism is delirium (66 per cent). There is no definite correlation between the level in the blood and the severity of the symptoms. Bromide acne cannot be considered as a definite criterion, as it is frequently not present with high levels in the blood and is occasionally present with very low levels. After discontinuance of the drug, the average duration of bromide intoxication is from two to six weeks, but it may vary within wide limits. Complicating factors, such as alcoholism, psychoneuroses and depressive and involutional psychoses, may obscure the diagnosis of bromide intoxication and may interfere with treatment.

DE JONG, Ann Arbor, Mich.

Diseases of the Brain

CASE OF FALSE LOCALIZING SIGNS OF CEREBRAL NEOPLASM. J. M. NIELSEN and A. E. HOLLENBECK, Bull. Los Angeles Neurol. Soc. **5**:124 (June) 1940.

In an arteriosclerotic, reputedly right-handed man who had had three episodes of hemiplegia, Nielsen and Hollenbeck found right hemiparesis, aphasia, Argyll Robertson pupils and a negative Wassermann reaction. Necropsy revealed a glioma in the right temporal lobe and an area of softening in the right side of the tegmentum of the pons. The false signs were explained as follows: The aphasia was due to the fact that the patient was originally left handed, the Argyll Robertson pupils to the softening in the tegmentum and the right hemiparesis to the pressure of the left side of the brain stem against the edge of the tentorium cerebelli.

MACKAY, Chicago.

DOMINANCE OF THE RIGHT OCCIPITAL LOBE. J. M. NIELSEN, Bull. Los Angeles Neurol. Soc. **5**:135 (Sept.) 1940.

Nielsen reports 2 cases bearing on the disputed question of unilateral dominance in the occipital lobes as regards associative, nonlanguage functions. In the first case a right-handed woman exhibited visual agnosia for objects and spatial disorientation resulting from a vascular lesion with shrinkage of the entire right occipital lobe. In the second case an elderly man with arterial hypertension experienced repeated cerebral vascular accidents over a period of nearly two years. Careful study revealed a close correspondence between the clinical manifestations and the lesions observed at autopsy. Visual verbal agnosia had been due to softening in the left supramarginal and angular gyri. Auditory verbal

agnosia had resulted from a severe lesion in the left temporal lobe. Left hemiplegia had followed softening in the right uncus. Left homonymous hemianopia and visual agnosia for inanimate objects had been due, respectively, to two lesions in the right occipital lobe.

In a previous study Nielsen had found 13 cases in the literature in which a unilateral occipital lesion had produced visual agnosia for objects. In 4 of these 13 cases the lesion was on the right side, a higher proportion than the normal incidence of left handedness (10 per cent) would suggest. The 2 cases described add emphasis to this disproportion. Nielsen suggests that the crossed left temporal and right occipital dominance may be due to the establishment of occipital dominance on the right before temporal dominance (dependent on language) is established on the left. Nature may then find it more economical to leave the right occipital lobe dominant than to establish new engrams on the left side.

MACKAY, Chicago.

ACOUSTIC NEUROMA PRODUCING TIC DOULOUREUX. W. D. ABBOTT and B. M. MERKEL, J. Iowa M. Soc. **30**:465 (Oct.) 1940.

According to Abbott and Merkel, only 18 cases have been reported in which neuroma of the acoustic nerve produced typical pain resembling that of major trigeminal neuralgia. A woman aged 30 was referred to one of the authors because of pain in the right side of the upper lip, nose and forehead. The pain was sharp and lancinating and was induced by touching the upper lip, talking or eating. Results of examination were negative except for a persistent trigger zone in the right side of the upper lip; touching this area produced pain in the first and second branches of the right trigeminal nerve. Inhalations of trichloroethylene were tried temporarily. The pain became more intense, and injection of alcohol into the first and second branches of the right trigeminal nerve was performed. This freed the patient from pain for about seven months, after which pain returned with the same radiation as previously. The corneal reflexes were present and equal on the two sides. A repetition of the injection of alcohol again rendered the patient free from pain. However, two months later vertigo, nausea and vomiting developed. Examinations of the ears, nose and sinuses revealed nothing abnormal. About a year after the second injection of alcohol the facial pain recurred, although there was still anesthesia in the first and second branches of the right trigeminal nerve. Because of the history of an acute Ménière's syndrome and persistent anesthesia in the affected branches, exploration of the posterior fossa was advised, with the possibility of an acoustic neuroma in mind. When the cerebellum was elevated, the fifth, seventh and eighth nerves were found stretched over a tumor the size of a large hazelnut. This was removed piecemeal, and the nerves were left intact. The microscopic examination revealed acoustic neurofibroma. Recovery was uneventful. The patient has been free from pain, and there has been a gradual return of the function of the facial nerve, so that she can close the eyelids and the nasolabial fold is present, but there is drawing of the angle of the mouth on smiling and she is unable to whistle. Examination sixteen months after the operation revealed complete return of sensation over the right side of the face. The authors think that when there is evidence of compression of the trigeminal sensory root and neighborhood signs, such as diminution or absence of the corneal reflex, Ménière's syndrome and loss of hearing accompanied by ataxia and incoordination of the extremities, it is well to consider the posterior approach to the sensory root. They stress that the more simple methods of inhalation of trichloroethylene and peripheral or deep injection of alcohol are not sufficient to produce permanent relief from pain, and they warn that there have been insufficient grounds to justify the sense of security which has been felt by advocates of the transtemporal approach to the posterior sensory root of the trigeminal nerve.

J. A. M. A.

HYPERACTIVE CAROTID SINUS REFLEX. B. E. GOODRICH, J. Michigan M. Soc. **39:** 768 (Oct.) 1940.

In a group of 84 persons suffering from what appeared to be a hypersensitive carotid sinus reflex, Goodrich was able to duplicate the attacks by pressure on the carotid bulb. Sensitivity varied, so that only in the degree of reaction, rather than in kind, were some persons abnormal. Sixty-five of the 84 persons were men. The complaint on entrance to the hospital ranged from a few transient dizzy sensations to repeated attacks of syncope. Dyspnea, substernal pain, numbness and weakness occurred. Blindness, aphasia and aphonia were reported. Four patients had only gastrointestinal effects, although many had associated gastrointestinal symptoms. Earlier in this study the patients were exhaustively examined, and many laboratory and technical tests were performed before a working diagnosis was made and treatment started. This consisted of advising patients to lessen spontaneous stimulation of the carotid sinuses by avoiding tight collars, abrupt motions, looking upward, singing and other activities leading to increased intracarotid pressure or to external mechanical stimulation. Medication to decrease the vagus reactions and to augment the activity of the sympathetic portion of the autonomic nervous system was utilized. Atropine or synthetic related drugs were most commonly used for vagus inhibition. Ephedrine sulfate, and in some instances amphetamine sulfate, was given and appeared to be helpful. Thyroid was employed in the majority of cases. Its administration was continued until all other medication was stopped. If no symptoms recurred, continued thyroid medication depended on evidences of thyroid need, judged independently of the carotid sinus activity. Demonstrating to the patient that the origin of the attacks was known and that they could be produced at will restored his confidence. Correction of undesirable habits and ways of living resulted in the cessation of symptoms in 1 instance without any medication. Fifty-three of the 84 patients were treated, and 32 were completely relieved, 13 were satisfactorily relieved (the major handicap was avoided), 5 required continuous treatment and 2 were not relieved; both of these had severe cerebral damage, and surgical denervation was not advised. Surgical denervation on the right carotid sinus of 1 patient brought about complete relief for one year, when symptoms recurred and the patient refused further treatment. The author concludes that hypersensitivity of the carotid sinus reflex becomes more frequent with advancing age and in persons with arterial hypertension. The symptoms are frequently considered heart attacks, and digitalis, which is often prescribed, further sensitizes the reflex and exaggerates the symptoms. Electrocardiographic records indicate that the vagal effect is involved in the more dramatic symptoms. J. A. M. A.

PARAPHYSIAL CYSTS OF THE THIRD VENTRICLE. HOWARD ZEITLIN and BEN W. LICHTENSTEIN, J. Nerv. & Ment. Dis. **91:**704 (June) 1940.

Cysts arising from the vestigial remains of the paraphysis in the anterior portion of the roof of the third ventricle may occlude (often intermittently) the foramens of Monro and impinge on the thalamic and hypothalamic nuclei, the optic chiasm and other neighboring structures. Early symptoms include sudden or intermittent headaches, somnolence, visual disturbances and convulsions, while later unconsciousness, mental aberrations, hyperthermia, paresthesias and weakness may occur. Zeitlin and Lichtenstein report the case of a youth aged 17 years who was suddenly seized with headache, vomiting, weakness and, later, strabismus. The next day there were hypersomnia, bradycardia, paralysis of the left internal rectus muscle and blurred optic disks. Cerebrospinal fluid pressure was elevated; the temperature rose to 104 F., and coma supervened, with loss of tendon reflexes. Death occurred two days after the onset of the illness. Autopsy revealed an ovoid cystic tumor, measuring 20 by 22 mm. in transverse diameters, attached to the roof of the third ventricle, which occluded the foramens of Monro. Microscopically, the wall of the cyst consisted of connective tissue lined within by one

or more layers of columnar epithelial cells possessing cilia. The cytoplasm was filled with granules and was frequently extruded into the cyst, forming a homogeneous, colloid-like material. The capsule was attached to the tela choroidea superiorly and to the choroid plexus.

MACKAY, Chicago.

THE PHENOMENON OF BODY ROTATION IN FRONTAL LOBE LESIONS. JOSEF GERSTMANN, J. Nerv. & Ment. Dis. **92**:36 (July) 1940.

On the basis of clinical and pathologic observations, Gerstmann describes rotation, or a tendency to rotation, of the body as a frequent, but not obligatory, sign of lesions of the frontal lobes. The phenomenon occurs only when the patient is upright and consists of circling movements of varying radius, but rarely of rotations around the vertical axis. The movements are directed toward the side of the lesion, seem voluntary but are probably involuntary, occur most readily when the feet are together and the eyes closed and are unaccompanied by vertigo or changes in the position of the eyes. Active or passive turning of the head toward the affected frontal lobe increases the tendency to rotation in the same direction. Turning of the head toward the unaffected side produces no reaction or may increase the rotation toward the affected side.

This phenomenon of the body rotation may be hidden or obscured by a frequently associated tendency of the patient to fall backward and away from the side of the lesion. With the unilateral lesions of the frontal lobes these rotary and falling movements are mutually antagonistic. Although body rotation may be seen in cases of lesions in other parts of the brain, its characteristics are then different. Lesions of the cerebellum and middle cerebellar peduncle may cause rotation which is away from, instead of toward, the side of the lesion and which occurs not only when the patient is standing but when he is lying or sitting. Rotation with the patient in the latter position is found also with parieto-occipital lesions. The reaction as described seems therefore to Gerstmann to have diagnostic value for lesions of the frontal lobe.

MACKAY, Chicago.

CEREBELLAR SUBDURAL HEMATOMA IN INFANT TWO WEEKS OLD WITH SECONDARY HYDROCEPHALUS. R. G. COBLENTZ, Surgery **8**:771 (Nov.) 1940.

Coblentz presents the history of an infant 2 weeks of age who recovered after an operation for an encysted subdural hematoma. The author believes that his is the first case in which such a lesion has been recognized during life and cured by operation. The hematoma was located over the right cerebellar hemisphere. Secondary hydrocephalus also was present. Although there was no definite history of trauma, ecchymosis of the upper lids and a moderate occipital caput led the author to suspect a slight trauma as the most likely etiologic factor. Prompt disappearance of blood in the lumbar subarachnoid fluid after daily lumbar punctures and continued increased intracranial pressure indicated a coexisting lesion. Subdural hematoma over the cerebral hemispheres was ruled out by subdural taps. Ventriculographic examination definitely located the lesion in the posterior fossa. Evacuation of the clot through a small trephine opening without drainage effected a cure. At the time of writing, the baby is 3 months old and has made a complete recovery.

J. A. M. A.

JUVENILE PARESIS [DEMENTIA PARALYTICA] IN ONE TWIN. REDVERS IRONSIDE, J. Neurol. & Psychiat. **3**:329 (Oct.) 1940.

Ironside reports a case of juvenile dementia paralytica in one member of dizygous twins, the syphilitic infection having been transmitted by the mother. The affected twin showed no stigmas of congenital syphilis except for general physical and mental retardation. At the age of 10 he began to show signs of physical deterioration and the Wassermann reaction of the blood was positive. From the age of 15 there was progressive mental deterioration characterized by

childishness, irritability and impairment of memory, speech and intellectual processes. Neurologic examination at the age of 17 disclosed ataxia, dysarthria, tremor, and a Babinski sign bilaterally, and examination of the cerebrospinal fluid showed changes characteristic of dementia paralytica. The healthy twin appeared normal on clinical and serologic examinations. The literature contains only 2 other reports of similar instances, 1 of a dizygous twin reported by Wile and Welton and the other of a possibly monozygous twin reported by McKendree. The explanation for the escape from infection of the healthy twin remains unknown.

MALAMUD, Ann Arbor, Mich.

DIAGNOSIS AND TREATMENT OF SWELLING OF BRAIN. M. DE CRINIS, Wien. klin. Wchnschr. **53**:637 (Aug. 9) 1940.

According to de Crinis, it is necessary to differentiate between swelling and edema of the brain. Swelling of the brain is an enlargement in volume which is not a direct result of hyperemia, cerebral edema or hydrocephalus. The chief difference between swelling and edema is that in swelling the water content of the brain is less and the consistency is greater than in edema. The increased volume in cases of swelling of the brain infringes on the available space, and choked disk, signs of vagal irritation (slow pulse and nausea) and headaches appear. For the necroscopic diagnosis of swelling of the brain it is essential that the examination be made shortly after death, for if considerable time elapses cerebral swelling may result from the postmortem absorption of cerebrospinal fluid. The macroscopically visible signs of swelling of the brain are flattening of the convolutions and reduction of the cerebrospinal fluid spaces and of the subarachnoid space; also, the consistency of the brain is increased, and it is comparatively dry and sticky. Swelling of the brain is regularly found after death during status epilepticus, status paralyticus, uremia and puerperal eclampsia, after sudden death in catatonic excitation and from lesions of the brain resulting from electrical injury and after death from inflammatory diseases of the brain, such as encephalitis and meningitis, and from cerebral abscess. In children who died suddenly, swelling of the brain has been known to be the only pathologic manifestation. The author gives particular attention to cerebral swelling associated with cerebral tumors. The swelling of the brain does not parallel the size of the cerebral tumor. Fist-sized tumors in the frontal portion of the brain may exhibit no signs of spatial limitation, whereas small tumors, the size of a cherry, may produce pressure and sudden death. Swelling of the brain with the acute signs of cerebral pressure often develops after transportation of patients with cerebral trauma or tumor. The incidence and extent of cerebral swelling are determined by the type of tumor. Tumors with infiltrating growth, such as gliomas, cause swelling more readily than circumscribed tumors. Meningiomas cause swelling of the brain only after they have reached a certain size. Swelling of the brain is rare in the presence of angiomas. The clinical symptoms of cerebral swelling may be fleeting at first, and they may not be limited to the immediate vicinity of the focus of the disease but may involve distant regions. The fleeting character and the mildness reveal that they are neighborhood or distant symptoms rather than focal or nuclear symptoms. Response to treatment may likewise be of help in determining whether symptoms are caused by pressure on the brain or by a tumor. The author discusses measures effecting dehydration which not only reduce the pressure on the brain but also permit a conclusion regarding the cause of the swelling. Urea plays an important part in tissue metabolism and in the physicochemical condition of the tissues. The author was able to demonstrate urea in the brain tissue of patients in whom cerebral tumor or abscess, encephalitis, status epilepticus or delirium tremens had produced swelling of the brain. He is convinced that swelling of the brain is chiefly a physicochemical problem. The living brain contains lipoids and protein bodies, which are in different states of swelling. The state of swelling is dependent on humoral, toxic and other influences. In swelling of the brain the tendency of the colloids to absorb water is increased

beyond physiologic limits. In edema of the brain the absorption tendency is reduced and water is given off. This differing physicochemical behavior of the brain colloids is due to pathologic processes, some of which are still unknown.

J. A. M. A.

Diseases of the Spinal Cord

ACUTE METASTATIC SPINAL EPIDURAL ABSCESS. DAVID L. REEVES, Arch. Surg. **41**:994 (Oct.) 1940.

Reeves reports 2 cases of acute metastatic lumbar epidural abscess in which operation was performed before evidence of compression had set in with complete recovery. Abscesses of the epidural space are believed to occur either by extension from a contiguous infection or by metastasis from a distant focus. The larger, more interesting group, that of hematogenous origin, presents a more difficult problem in diagnosis. These abscesses almost always occur posteriorly. This is due to the fact that the epidural space is present only dorsal to the nerve attachments, while ventrally the dura is everywhere closely attached to the bones of the vertebrae and their ligaments. Epidural abscesses are most common in the lumbar and thoracic regions, the epidural space being larger in these areas and only potential in the cervical region. With few exceptions, the pyogenic organism associated with these infections is the staphylococcus. Although there is variation in the symptoms, depending on the location of the abscess, the history is rather uniform. Usually the story of some previous infection, such as furunculosis, can be obtained. Commonly, within the first few weeks following such an infection the patient complains of a boring pain in the spine, accentuated by straining or movement. The disease assumes the character of a toxemia, with fever and leukocytosis. Radicular pain becomes evident; the spine and neck are rigid, and the Kernig sign is positive. Extreme tenderness of the spinous processes over the affected area, as well as spasm of the adjacent back muscles, is elicited on examination. Either gradually or suddenly thereafter, evidence of involvement of the cord becomes apparent, with paraplegia, sphincteric disturbance and sensory loss. A lumbar puncture and a Queckenstedt test are essential to confirm the diagnosis. When the infection is in the lumbar region the spinal puncture is apt to evacuate pus, and care must be taken not to initiate meningitis. The thoracic epidural abscesses produce early block, and Froin's syndrome is commonly present. With few exceptions every patient with an undiagnosed and surgically untreated abscess of this type has died. The prognosis depends largely on early diagnosis, laminectomy and drainage. If these are achieved the chances for recovery at least are hopeful. Should the diagnosis be established after complete paralysis has set in, laminectomy may lead to recovery and relief of pain but seldom leads to return of function of the affected muscles.

GRANT, Philadelphia.

INTRADURAL SPINAL LIPOMAS. GEORGE WILSON, HARVEY BARTLE JR., and JAMES S. DEAN, J. Nerv. & Ment. Dis. **91**:745 (June) 1940.

Wilson, Bartle and Dean report the case of a woman aged 21 who began to have pain in the lower left side of the chest, followed a month later by progressive numbness and weakness in the lower extremities. Examination two months after the onset revealed marked spastic paraplegia with severe impairment of deep sensibility in the legs. The spinal fluid was yellow, contained much protein, reduced Fehling's solution and gave a colloidal gold reaction of 4555555555. Jugular compression increased the spinal fluid pressure but reproduced the pain in the chest. Superficial anesthesia and anhidrosis rapidly appeared below the sixth thoracic dermatome, and the paraplegia became complete. At operation a smooth, intradural, fatty tumor was found firmly attached to the dorsal surface of the cord. A small portion was removed for biopsy, and death occurred three months later. Autopsy revealed a large fibrolipoma, apparently arising beneath the pia-arachnoid and replacing the spinal cord except for a U-shaped ventral rim, the

inner border of which was partially lined with ependyma, "as though an open syringomyelia existed." Edema and degeneration were observed in the remaining portions of the spinal cord, and the overlying meninges were greatly thickened. The authors believe that the lipoma arose from the connective tissue of the pia-arachnoid by metaplasia and grew out from the cord rather than into it. They mention another case in which a small mixed tumor, containing several tissues of mesodermal origin, was found between the mamillary bodies in the brain of a cretin.

MACKAY, Chicago.

FAMILIAL LUMBOSACRAL SYRINGOMYELIA. C. VAN EPPS and H. D. KERR, Radiology **35**:160 (Aug.) 1940.

The appearance at the clinic of two or more members of four different families with trophic changes in the soft and bony tissues of the feet led Van Epps and Kerr to review the literature of similar cases. It is their belief that the various etiologic factors of the syndrome are of the developmental type and that the terms status dysraphicus myelodysplasia, syringomyelia and trophopathia pedis myelodysplastica all have some basis. They have classified their cases in the syringomyelia-group and feel that the term "familial lumbosacral syringomyelia" is the best designation. To date there have been reported 54 cases, to which the authors now add 27 of their own, making a total of 81 cases. They made examinations in 19 of the 27 cases included in this report. Twenty-six of these cases occurred in four families, while in the other case the authors have been unable as yet to establish a familial tendency. Of the 19 cases in which examination was made, the feet showed calluses in 16, one or more ulcers in 17 and pain, usually slight, in 6. The knee jerks were normal in 18; the achilles tendon reflex was absent in 12, and plantar extension was absent in one or both feet in 9. Pallesthesia was impaired or lost in 16 cases; hyperkeratosis was present in the hands in 2 cases, and the skin of the hands was dry and thick in a third case. Roentgen examination of the feet showed osseous changes in 15 cases. These changes were trophic in character—absorption of bone, disintegration of joints, periosteal new bone and pathologic fractures. Soft tissue changes could also be seen. Films of the lumbosacral portion of the spine convinced the authors that spina bifida occulta per se is not a necessary part of the syndrome. In 4 cases there were episodes of severe infection. In 1 case of chronic infection amputation below the knee was necessary. In only 1 case has there been a possible appearance of the condition in the fourth generation. One family showed an associated case of striate diplegia with athetosis. In the sporadic case there were unequal partial Argyll Robertson pupils, primary optic atrophy, and retrobulbar neuritis with slightly constricted fields. This case may be one of tabes, but the authors have included it because they have not seen similar changes in the feet occurring in tabes and because these changes are typical of those in the familial groups. They reach the conclusion that the occurrence of chronic painless ulcers on the feet, especially when associated with roentgen evidence of neurotrophic changes in the bones and joints of the forepart of the foot, should lead to a study of the family history in a search for similar cases. Familial lumbosacral syringomyelia is one of the most frequent causes for such a syndrome. Irradiation of the lumbosacral cord appears to be the best available treatment.

J. A. M. A.

SYMPTOM OF NARROWED INTERVERTEBRAL DISK. H. SCHAER, Schweiz. med. Wchnschr. **70**:849 (Sept. 7) 1940.

Schaer directs attention to the fact that narrowing of the intervertebral disk is frequently encountered in diseases of the vertebral column. It is observed as an accompanying symptom of numerous degenerative changes of the intervertebral disk or of the adjoining vertebral bodies in the frequently occurring spondylosis deformans. It is seen as a characteristic sign in juvenile kyphosis, in kyphosis of the aged and in osteoporosis of the aged. In all these conditions the narrowing involves all or several of the disks. The narrowing of an isolated intervertebral

disk occurs much less frequently and is difficult to diagnose. The author describes several cases in which this symptom was present and discusses the underlying pathologic process. Isolated narrowing of an intervertebral disk is due either to a reduction in its volume as the result of primary degeneration of the disk itself (osteochondrosis) or to pathologic processes in the surrounding tissues. The narrowing is found chiefly as an early roentgenologic symptom of tuberculous spondylitis. It is the result of the breaking through of the still intact intervertebral disk into a circumscribed diseased area of the adjoining vertebra. The deformation resulting from this breaking through leads to a seeming contraction, which at times is regular and at others irregular and which is frequently accompanied by a dorsal displacement of the vertebra above it. This early symptom of tuberculous spondylitis corresponds to the anatomic stage of the cavernous destruction of the vertebral body, a fact that has to be considered in estimating the age of a tuberculous process in the vertebral column.

J. A. M. A.

Peripheral and Cranial Nerves

DYSPHAGIA WITH DISORDERS OF THE HEART AND GREAT VESSELS. ARTHUR L. BLOOMFIELD, Am. J. M. Sc. **200**:289 (Sept.) 1940.

Bloomfield reports a case of dysphagia occurring in a Chinese waiter aged 37 who complained of shortness of breath, pain and difficulty in swallowing. There were classic signs of mitral stenosis, with great enlargement of the heart. It was thought that the dysphagia was due to spasm of the esophagus, secondary to pressure by the large auricle, rather than to actual obstruction. Dysphagia may occur in connection with many disorders of the heart and aorta. While compression of the esophagus by a dilated left auricle often occurs, clinical dysphagia from this cause is exceedingly rare. Dysphagia with pericarditis seems to be a rare event. Actual difficulty in swallowing probably occurs only when the esophagus is compressed by a large effusion. Hence, in the presence of pericarditis, dysphagia may be of practical diagnostic importance as to the amount of fluid present. Dysphagia is recognized by all to be a frequent symptom of saccular aneurysm. Dysphagia by compression occurs with right-sided aortic arch, double aortic arch and aberrant right subclavian artery. In cases of dissecting aneurysm, pressure on the esophagus by the false sac must be a common event but clinical dysphagia rarely occurs. Dysphagia in a supposed case of coronary occlusion should arouse suspicion of dissecting aneurysm.

MICHAELS, Boston.

RELATION BETWEEN MULTIPLE PERIPHERAL NEUROPATHY AND CIRRHOSIS OF THE LIVER. EDGAR WAYBURN and CATHERINE R. GUERARD, Arch. Int. Med. **66**:161 (July) 1940.

Wayburn and Guerard report on the relation between multiple peripheral neuropathy and cirrhosis of the liver in 272 cases of cirrhosis of the liver which they studied. Peripheral neuropathy was diagnosed in 17 per cent of the cases. An increase in the number of cases recognized was thought to be due to the interest in the disease.

Early cirrhosis was seen more often in the group of patients with peripheral neuropathy because it may have been the patient's chief complaint or it may have imposed an additional set of symptoms to make the patient seek medical aid. Cirrhosis accompanied by peripheral neuropathy is more common in females, whereas cirrhosis alone is found predominantly in males.

The connection between peripheral neuropathy and cirrhosis of the liver was so frequent that it may be of some importance in throwing light on the cause of the latter condition, since vitamin B deficiency may be related to disease of the liver. It is possible that part of the vitamin B complex may contain a liver-protective factor. In experimental animals on a diet deficient in vitamin B complex but adequate in riboflavin, vitamin B_1 and vitamin B_6 hepatic damage varying from

fatty degeneration to cirrhosis developed. This could be prevented by adding yeast to the diet. The factors of inadequacy of the diet and decreased intestinal absorption seem to be of importance in the group of patients with a history of alcoholism.

Treatment with concentrated vitamins, particularly vitamin B, produced regression in the peripheral neuropathy. The general condition of the patient with cirrhosis often improved at the same time.

BECK, Buffalo.

RETROBULBAR NEURITIS. F. D. CARROLL, Arch. Ophth. **24**:44 (July) 1940.

Carroll reviews the data on 100 patients with retrobulbar neuritis observed during four years and examined by him. He excluded from the series 65 patients with "toxic amblyopia associated with deficient diets or with excessive use of tobacco or alcohol whom he encountered during the same period. Also excluded from discussion is toxic amblyopia produced by known toxic agents; lead, arsenic and thallium. Complete neurologic, roentgenographic, allergic and medical examinations were carried out so that an etiologic diagnosis could be established. The average age of the patients when first examined because of blurred vision was 32.7 years; the extremes were 7 and 70. The causative factors in the 100 cases seemed to be: multiple sclerosis in 37, Leber's disease in 9, encephalomyelitis in 8, arachnoiditis in 3, vascular disease in 3, sinusitis in 2, syphilis in 2, postspinal anesthesia in 1 and neuromyelitis optica in 1. The cause of the retrobulbar neuritis was not determined in 34 cases. If the etiologic agent is known, treatment should be directed toward its elimination. When it is unknown, treatment is of questionable value. Hospitalization during the acute attack is probably advisable. Tumor of the brain and tobacco-alcohol amblyopia are to be differentiated from retrobulbar neuritis. Most patients noticed sudden decrease of vision in one eye. Sometimes this was observed on waking in the morning and sometimes while working or playing. The vision grew worse after the first change. A few patients reported loss of sight in one eye or in both eyes with no further change or with subsequent slight improvement. A few patients stated that vision had decreased in the two eyes gradually and at about the same rate. The two eyes of 78 patients were involved, often not at the same time. Many patients complained of a large blindspot in the center of vision, and some with bilateral blindspots stated that they saw better in dull light. Pain was an important symptom. Twenty patients volunteered the information that the involved eye was painful on movement; others admitted having pain when questioned. The eyeball was often tender to palpation. Sometimes pain was referred to as "deep" or "behind the eyeball." Other patients had severe headaches at the time of onset. The cause of the headaches is speculative. Mild, localized meningeal involvement may be the cause in some cases. The visual acuity in the involved eyes was markedly reduced in most instances. The characteristic field change was a central scotoma. There was usually no change in the normal appearance of the disks in the early stages of the disease. Blurring of the margins of the disk occurred sometimes. Pallor of the optic nerve usually developed temporally after a few weeks. The unreliability of contraction of the pupil to light as a sign of retrobulbar neuritis was indicated by its demonstration in several normal eyes.

J. A. M. A.

RECURRENT POLYRADICULONEURITIS (GUILLAIN-BARRÉ VARIETY) WITH PSEUDOTABETIC SYMPTOMS. MICHEL ANDRÉ, J. belge de neurol. et de psychiat. **40**:28 (Jan.) 1940.

André reports the case of a man aged 33 who had, at an interval of four years, two periods of illness with identical symptoms and signs—paresthesias, pseudotabetic ataxia and absence of tendon reflexes with preservation of cutaneous reflexes. There was albuminocytologic dissociation in the cerebrospinal fluid. The patient made a complete recovery from each illness. A diagnosis of polyradiculoneuritis of the Guillain-Barré type was made. Very few instances of the Guillain-Barré syndrome have been described in which there was recurrence of symptoms.

DE JONG, Ann Arbor, Mich.

PAIN IN AMPUTATED STUMPS. E.-P. LECLERC, Presse méd. **48**:667 (Aug. 21-24) 1940.

Leclerc employed procaine hydrochloride, simple nerve resection and lumbar sympathectomy in treating pain in amputation stumps. Procaine hydrochloride, though only rarely affording permanent relief, is regarded by the author as valuable in indicating further therapy. For amputations of recent date and with localized pain, procaine hydrochloride gives good temporary results. In cases of long-standing and aggravated pain, in which the drug was unable to prevent recurrence, satisfactory results were obtained by lumbar sympathectomy for the lower extremity and by ablation of the stellate ganglion for the upper extremity. In the mixed type of stump pains in which the remaining stump was involved, as well as the removed anatomic portion, as a result of hyperesthesia, a favorable analgesic action of the drug indicated resection of the sympathetic chain and ganglia. If this operation was ineffective, a simple nerve resection followed by prompt suture or grafting gave relief. This supplementary operation was not often necessary. An adequate interval of time, however, must then be allowed not only to avoid further damage to the patient but to gage the efficacy of the first operation. Lumbar sympathectomy, performed by the author in a limited number of cases, achieved remarkable results in relieving formication and vasomotor disorders. The author cites a remarkable case in which multiple operations had been performed for frozen feet since 1917. When seen in 1935, the patient was suffering agonizing pain. The stump indicated vasomotor and trophic dysfunction and presented a neuroma at the site of the cicatrix. Lumbar sympathectomy was done, and all pain ceased on the evening of the same day, not to recur. When seen in 1939, the patient was well and had qualified as a gamekeeper, though before that he had been unable to endure any artificial apparatus. The author obtained better results by resection of the sympathetic chain and ganglia, done either as the first operation or in order to correct unsatisfactory previous results, than by all other therapeutic procedures, especially in the thoroughness with which the whole clinical picture was altered. This operation was the procedure of choice whenever procaine hydrochloride was observed to alleviate pain. Simple nerve section for control of imaginary nostalgic pain in the severed limb, followed by prompt nerve reconstitution after use of phenol at the central termination, was tried and abandoned for the method of choice. Periarterial sympathectomy, except in 1 case, yielded only temporary relief. Early intervention offers the best result. J. A. M. A.

Treatment, Neurosurgery

REMOVAL OF LONGITUDINAL SINUS INVOLVED IN TUMORS. WALTER E. DANDY, Arch. Surg. **41**:244 (Aug.) 1940.

The neurosurgeon is frequently faced with the problem of a tumor of the brain, always a dural meningioma springing from the falx near the midline, which has invaded the longitudinal sinus. Complete removal of the tumor demands ligation and excision of that part of the sinus involved by the tumor. Interference with the blood supply of the cerebral hemispheres, with serious neurologic sequelae, can result. However, in dealing with bilateral tumors, and frequently with unilateral tumors, the longitudinal sinus is often occluded either by compression of the tumor or by direct invasion. Consequently, removal of a section of the sinus adds little or nothing to the demand for a collateral venous circulation. In these cases the venous obstruction has doubtless been gradually progressive and because of this there has been time for the collateral circulation to develop. Whether a patient's sinus could be similarly resected can only be conjectured; there is no evidence from the literature to support or refute such a claim.

Dandy has reviewed the literature and discovered 9 cases of resection of the longitudinal sinus. In 3 of these cases the resection was made anterior to the rolandic vein. In 1 instance a posterior section of the longitudinal sinus, together

with a part of one transverse sinus, and the tentorium were removed. The author adds 4 cases from his own experience. In 2 of these resection was made in the most anterior part of the sinus and in 2 posterior to the the rolandic vein. In 2 of the cases the sinus was excised when the tumor had recurred, and in 2 the sinus was removed at the first operation, when the tumor was known to be bilateral. In all of these cases in which occlusion of the sinus had occurred prior to resection no neurologic signs appeared which could be attributed to this important step in the operative procedure. But there is no available evidence by which it can be known whether the longitudinal sinus can be removed in part before gradually progressive occlusion has occurred.

GRANT, Philadelphia.

SURGICAL MANAGEMENT OF SACROCOCCYGEAL AND VERTEBRAL CHORDOMA. CHARLES G. MIXTER and WILLIAM JASON MIXTER, Arch. Surg. **41**:408 (Aug.) 1940.

Chordoma is a tumor arising from the remnant of the notochord. It may occur anywhere in the cerbrospinal axis, from the sphenoid bone to the coccyx. In order of frequency, it is found in the sacrum, the base of the skull and the lumbar portion of the spine, but it may occur in any of the vertebrae. If vertebral in origin, the tumor usually arises in the vertebral body. Chordomas are difficult to eradicate on account of the usual antevertebral position, the bony origin, the intimate relation to the spinal nerves and, at times, the actual invasion of the dura and spinal cord. Thus block excision is applicable only to the lesions in the sacrococcygeal region, which fortunately are the most numerous. Such tumors should lend themselves to block removal unless they have progressed too extensively, for they usually show a tendency to remain encapsulated, to recur locally and to metastasize late in the disease. They are of more common occurrence in the lower part of the sacrum or in the coccyx than in the upper segments of the sacrum. Very rarely does invasion of the rectum or of the bladder take place. The differential diagnosis of chordoma of the sacrum depends in great measure on roentgen examination, but even with such examination there is room for error at times. One should suspect chordoma whenever a tumor is found which causes severe pain and appears to arise from the sacrum. The tumor may be confused with sarcoma, osteoma, ependymoma of the filum terminale, carcinoma of the rectum with involvement of the sacrum, metastatic carcinoma or tumor arising from the generative organs. One should remember that chordoma seldom ulcerates through into the rectum, though this condition is sometimes reported, as in intestinal obstruction. The tumor is usually smoother, more elastic and more discrete than the malignant tumors just mentioned. Osteoma, on the other hand, is excessively hard. The roentgen findings may be definitely suggestive. A smooth-walled area of bone destruction, usually near the midline, with a homogeneous soft tissue mass bulging out from the region of the defect, is characteristic. The diagnosis is conclusively established only by biopsy in many instances. The soft, gelatinous tumor lends itself to aspiration, and the diagnosis has been frequently proved by this means. At operation the tumor is very vascular, and after the capsule is entered the mass is usually found to be soft and translucent. It is very friable and is slightly yellowish after it is separated from its blood supply. The capsule is a definite structure, and there is a sharp line of demarcation between the tumor and the surrounding tissues. The characteristic picture, microscopically, is that of a more or less homogeneous mucoid intercellular substance with widely separated strands or masses of large vacuolated cells. Mitoses are rarely seen.

The three methods of treating chordoma are by irradiation alone, by operation combined with irradiation and by operation without irradiation. Although occasionally irradiation, either with roentgen rays or with radium, may be beneficial, in general the tumor is radioresistant, and little if any improvement may be expected to follow treatment. It would appear that radical extirpation of sacrococcygeal chordomas offers the best chance of prolonged relief in spite of the high operative mortality in this procedure. It is not known whether it would be feasible to resect the upper two segments of the sacrum. Such an operation

would be very difficult and even if successfully carried out would cause great disability. It is possible to resect the sacrum below this level. Such an operation should not be considered if disease of the upper part of the sacrum is too extensive. Careful roentgen examination will determine this. Other contraindications of this type of operation are involvement of the sciatic nerve and evidence of distant metastases. To diminish the hazard of sepsis at the time of operation and in the postoperative period a preliminary colostomy has many advantages. It should be a defunctioning procedure and yet one that is readily capable of reconstruction should there be no indication for a permanent colostomy after the resection is accomplished. After the abdomen is opened and before the colostomy is done, the peritoneal cavity, the paravertebral lymph nodes and the liver should be examined for direct extension or metastases. A colostomy of the Devine type established in the sigmoid flexure of the colon permits preoperative cleansing of the distal segment and will relieve symptoms of obstruction if present. As soon as the colostomy is functioning well the sacrum is approached from behind. A block resection is carried out, with removal of all the structures involved, including the coccyx and the sacrum to a point definitely above the upper limit of the growth as previously determined by roentgen examination. The first and second sacral nerves will not come into the field of this procedure. One should sacrifice all the lower sacral nerves without hestitation rather than run any risk of cutting into the growth. Piecemeal removal is to be avoided, not only on account of the danger of recurrence but because of the extreme vascularity of the tumor. The vessels entering these growths are large, and careful hemostasis is important to prevent undue loss of blood. Should resection of the rectum be necessary or should injury occur during operation, the preliminary divergence of the fecal stream reduces the danger of serious infection to a minimum. With a well functioning colostomy and constant drainage of the bladder, the discomfort of the patient is reduced, the after-care simplified by elimination of use of the bedpan and the danger of wound contamination diminished. If the third sacral nerves and all below are cut there will be a considerable area of saddle anesthesia extending forward over the perineum and the external genitalia. There probably will be some loss of function of the anal sphincter, but immediate postoperative lack of function is not necessarily permanent. Vesical retention may occur, as after any pelvic procedure, and constant drainage is advantageous. Ultimately the sphincter of the bladder should be competent, though too little is known about the exact level of function of the bladder to enable one to be dogmatic on this point. It will be found that the gluteus muscles cannot voluntarily be drawn together after the removal of the lower part of the sacrum. The fact that part of the origin of these muscles is left free seems to cause little if any disability.

Chordoma of the vertebral column presents a very different problem from chordoma of the lower part of the sacrum and the coccyx. It is rare indeed that a preoperative diagnosis can be made with any certainty. The outstanding features of these growths are similar to those of extradural benign tumor of the spinal canal or of some destructive lesion of the vertebral body. In common with these growths, they usually cause compression of the cord or of the cauda equina with the signs associated with such compression, namely, pain, paralysis below the level affected and block of the spinal fluid. A history of trauma is somewhat suggestive. Chordomas grow more slowly than do malignant lesions. The roentgen picture, while not as characteristic as that of sacrococcygeal chordoma, may be helpful. If the body of the vertebra is involved there may be a rounded cavity visible in it, or there may be an irregular mottled appearance similar to that seen in vertebral hemangiomas except that the mottling is coarser. There is no evidence of new bone formation, as in metastatic carcinoma of the prostate; bone destruction is not as intense, nor does it show the moth-eaten appearance characteristic of most of the other forms of malignant disease of the vertebral body. The problem of treatment is also different. In the spine one is dealing with a growth which on account of its position is not open to radical extirpation. Therefore palliative operation and, if desired, roentgen therapy are the only

measures. These tumors are of slow growth. There is a definite tendency to dislocation or to collapse of the vertebral body. When the disease is extensive it is believed that after exploration and as complete removal of all tumor tissue as is possible, an early fusion operation should be performed to combat this danger.

GRANT, Philadelphia.

BUCCAL NEURALGIA: A FORM OF ATYPICAL FACIAL NEURALGIA OF SYMPATHETIC ORIGIN. FREDERICK LEET REICHERT, Arch. Surg. **41**:473 (Aug.) 1940.

Buccal neuralgia, a form of atypical facial neuralgia, is characterized by a burning, boring, aching, throbbing pain in the region of the lip, cheek, gum, tongue, maxilla, nose and upper and sometimes lower jaw, spreading at times to the zygoma, into or behind the eyeball or into the temporal region. Anatomic dissection has demonstrated sympathetic fibers from the carotid sinus following the arborization of the facial artery and vein. Extraction of teeth and injection of alcohol into branches of the trigeminal nerve give no relief.

Reichert reports on a series of 30 patients suffering from buccal neuralgia. Tic douloureux of one or more branches of the trigeminal nerve was associated with buccal neuralgia in 10 patients. Three patients with buccal neuralgia had hypothyroidism. The neuralgia was relieved by administration of thyroid extract and vitamin B. Buccal neuralgia was cured in 5 of 8 patients in whom the cervicothoracic portion of the sympathetic chain was interrupted. It was relieved in 13 of 17 patients by the simpler procedure of division of the sympathetic fibers running with the facial artery and vein at the lower border of the mandible.

GRANT, Philadelphia.

PNEUMOENCEPHALOGRAPHIC TREATMENT OF EPILEPSY. FAUSTO GUERNER, Arq. Serv. assist. psicopat. Estad. São Paulo **4**:5, 1939.

Fifteen patients with epilepsy were treated by the removal of spinal fluid and the insufflation of air. Suboccipital puncture was used in all cases. Fifty to 100 cc. of spinal fluid was removed and 40 to 100 cc. of air introduced. In 1 case only 20 cc. of air was used. All the patients had severe epilepsy of many years' duration. Four of them had evidence of focal cerebral disease in the nature of infantile hemiplegias and 1 crural monoplegia. All the patients showed severe mental changes. In none of the patients was there any evidence of increased intracranial pressure. No serious complications followed the pneumoencephalographic procedure in any case. Vomiting, headache, pain in the head and face, hyperhidrosis, torpor and restlessness were all transitory.

A daily record of attacks was kept before and after the encephalographic treatment. There was a definite and significant decrease in the number of attacks in 12 cases. In 4 cases there was a decrease of more than 50 per cent (maximum 65.5 per cent); in 6 cases the decrease was between 20 and 50 per cent and in the other 2 less than 20 per cent. In 3 cases there was an increase in the number of the attacks. The author considers this method of some therapeutic value and recommends its use as a last resort.

SAVITSKY, New York.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

SAMUEL B. HADDEN, M.D., *Presiding*

Regular Meeting, Oct. 15, 1940

An Interesting Reflex Response Associated with Parasagittal Meningioma: Report of a Case. DR. MICHAEL SCOTT.

A case is presented with motion picture demonstration of the reflex responses of a woman aged 63 who had complained of right-sided headache, tinnitus and difficulty in walking for the past two years. Percussion of the plantar surfaces of the right foot elicited the following phenomena: Whenever the metatarsal areas over the ball of the right foot or the tendons inserting into the lateral, medial or dorsal surface of the right foot were percussed or the toes were flipped, there was an immediate plantar flexion of the left foot, most marked in the toes. If the left knee was held flexed while the right foot was percussed, the flexion in the left foot was limited to the toes and was most marked in the left big toe. There was no fanning.

When percussion of the left foot was done in a manner similar to that of the right, there was no movement of the right foot and toes. There was, however, an active defense movement in the left foot when it was percussed. There was dorsiflexion of the foot and toes with flexion at the knee and thigh at times. Repeated examinations did not produce a Babinski or a Chaddock sign or ankle clonus. There was, however, marked dorsiflexion of the right big toe when the right tibia was stroked or the right gastrocnemius muscle compressed. This was not obtained on either side when similar stimuli were applied to the left leg. Percussion of either hand did not produce any of the phenomena observed on percussion of the foot or leg.

Evaluation of the clinical picture established the diagnosis of neoplasm of the right parietal lobe. At operation, Dr. Temple Fay observed a tumor about the size of an orange attached to the falx in the region of the corpus callosum. The microscopic diagnosis was xanthochromic meningioma.

After operation and until the patient was discharged, fourteen days later, the crossed reflex response was absent.

DISCUSSION

DR. S. F. GILPIN JR.: I do not believe the moving picture demonstrated the actual degree of plantar flexion in the toes. I can attest to the presence of this reflex. This is one of the contralateral reflexes which occur in some patients, similar to the adductor response associated with an active knee jerk on the opposite side. Perhaps Fulton would say that the vessels supplying the premotor area were compressed.

DR. JOSEPH YASKIN: It is difficult to explain this reflex. I can see that pressure produces a reflex, but why the crossed reflex? Why was there no Babinski sign? It is my impression that there is evidence of pathologic flexion in the left foot. I believe it is well recognized that the Babinski sign can be elicited on the opposite side as the result of stimulation of the foot.

DR. MICHAEL SCOTT: I can assure you there was no exchange of pathologic flexion; this was unquestionably a direct, brisk flexion of the toes.

Tic of Diaphragm (Postencephalitic): Bilateral Phrenicectomy, with Observations on Regeneration of Nerves and Description of a New Method of Thoracotomy and Transthoracic Phrenicectomy. DR. PENN-GÅSKELL SKILLERN (by invitation), South Bend, Ind.

This paper is based on a ten year study of a rare case of spasm (tic) of the diaphragm following epidemic encephalitis. When the patient was first seen, a search of the literature revealed but 2 reports of a similar condition, in neither of which, however, had the treatment resulted in ultimate cure. Since then several more cases have been reported, but in none of these, either, was ultimate cure effected. The patient in the present case was so tormented by the ever present spasms that a permanent cure was imperative. In attempts to effect such a cure, an unforseen accident (inadvertent tearing of one nerve at the superior aperture of the thorax) arose, which lent much more interest to the case but which, owing to the unflagging cooperation of an intelligent patient, was eventually rectified so that permanent cure was the ultimate result. To accomplish this, however, it was necessary to plan and execute a hitherto undescribed operative procedure, namely, transthoracic phrenicectomy. During this time unusual opportunities arose for the study of nerve regeneration. The history of the patient, together with an account of the first three operations and a review of the literature up to that time, has been published (Tic of Diaphragm [Postencephalitic] Relieved by Resection of Phrenic Nerves, *J. A. M. A.* **96**:2098-2099 [June 20] 1931).

When first seen in my office, the patient, a housewife aged 37, exhibited spasms of the diaphragm at the rate of about 200 a minute. At the first operation, 2 cm. of each phrenic nerve was resected, with disappearance of the spasms. They recurred, however, about nine months later. At the second operation the left phrenic nerve was ablated to the diaphragm, with disappearance of spasms. They recurred eight weeks later. At the third operation it was found that the right phrenic nerve was regenerated but was no larger than a coarse, white hair. In attempting to ablate the thoracic portion of this nerve, it was torn at the superior aperture of the thorax, and the attempt had to be abandoned.

After a lapse of six years the patient returned with spasms, which had recurred nine months after the last operation; fluoroscopic examination revealed that the right side of the diaphragm was involved, the left being still. There now followed three more operations to remove the delicate regenerated portion of the right phrenic nerve, with as many recurrences at the regular nine month interval. At the sixth operation an attempt was made to obliterate the bed occupied by the nerve by suturing together the roughened adjacent surfaces of the scalenus anticus and the sternocleidomastoid muscles, with the use of through and through sutures of heavy silk. Nevertheless, recurrence of spasms appeared four months after the sixth operation.

The only plan of permanent relief now available was obviously that of ablation of the thoracic segment of the phrenic nerve by a transthoracic route, that is, transthoracic phrenicectomy, an operation of which no record could be found. This was accordingly done by an original technic, the details of which will appear in the complete article to be published later. The entire thoracic portion of the right phrenic nerve was exposed and removed, together with the spray of terminal branches to the diaphragm, with of course permanent relief from the spasms.

(A moving picture of the spasms was shown, and is available to those who are interested.)

DISCUSSION

DR. WALTER E. LEE: In anticipation of this discussion, I took up the matter with Dr. Batson, professor of anatomy in the Graduate School of the University of Pennsylvania. He referred me to the experimental work of Greenmann (*J. Comp. Neurol.* **23**:479 [Oct.] 1913) on the regeneration of the peroneal nerve of the albino rat following section; this observer counted 100 fibers before operation and an average of about 250 fibers after operation. The work of Greenmann was corroborated by Dogliotti (*Arch. ital. di chir.* **34**:781, 1933; *J. de chir.* **45**:30 [Jan.] 1935). From this it would seem that the regeneration of the phrenic

nerve which Dr. Skillern observed after his first operation was to be expected and that avulsion is the only certain method of completely and permanently destroying the function of a nerve.

DR. A. M. ORNSTEEN: The surgical attack on this problem is out of my ken, but I appreciate Dr. Skillern's presentation as both instructive and based on sound surgical principles; results, however, are not consonant with neurologic concepts. Dr. Skillern mentioned the rarity of diaphragmatic tics, and with this there can be no disagreement, although I have about 6 such cases in my motion picture collection of postencephalitic disorders. In 1 of my cases Dr. Muller froze both phrenic nerves and obtained complete and permanent arrest of the hyperkinetic phenomenon, but parkinsonism eventually developed. Postencephalitic tics in the respiratory field may be limited to the diaphragm or the soft palate or may involve the accessory muscles of respiration.

I believe that in explanation of the recurrences in Dr. Skillern's case one is concerned not so much with primary degeneration of the phrenic nerve following sectioning or freezing and subsequent regeneration but with the hyperkinetic releases as a result of basal ganglion disease. The purpose of freezing, avulsing or sectioning the phrenic nerve is to break temporarily the peripheral motor reflex arc so that the abnormal discharges from the lower motor centers of the brain are interrupted, with the hope that when the phrenic nerve regenerates the hyperkinetic symptom will not recur. Fortunately, this has been the experience of most observers, but occasionally one may expect to meet with the unfavorable result encountered in the case of Dr. Skillern. The explanation may be found in the fact that after a postsurgical latent period following section of the phrenic nerve the abnormal motor impulses may reach the diaphragm through the thoracic spinal nerves.

DR. MOSES BEHREND: I got the same impression as did Dr. Ornsteen, that there was only a temporary break in the pathway to the diaphragm and that a collateral innervation to the diaphragm existed. I should like to speak of the technical surgical procedure in this case, and I might add that only an anatomist like Dr. Skillern could devise an operation of this sort to reach the phrenic nerve. It would seem to me much simpler to make a transverse incision in the third intercostal space. With the Rienhoff rib spreader the phrenic nerve is easily exposed. This technic is used for lobectomy and pneumonectomy.

DR. PENN-GASKELL SKILLERN: My interest in regeneration of nerves dates from the days of my assistantship to the late Dr. John B. Murphy, who, as is known, did a good deal of experimental work on the surgery of the nervous system. Axons have a great affinity for each other. Thoma was the first to call attention to the affinity, or positive chemotactic attraction, between cells of the same histologic structure. It was demonstrated that these axons will penetrate ordinary loose connective tissue for some distance to meet each other. When a nerve has been cut and placed in contact with a muscle that runs parallel to its long axis, the axon will span a still greater distance. If there is a mass of connective tissue ¼, 1/6 or even 1/32 inch (0.64, 0.42 or 0.09 cm.) thick between the ends no union will result. This interposition of fibrous tissue, which forms an impenetrable barrier across the path of the growing axons, explains many failures of union. It was for this reason that at the sixth operation I had hoped to prevent reunion of the nerve ends.

Nerves regenerate at the rate of about 1 mm. a day—hence the many months that elapse before reunion takes place. In cases like mine the only permanent relief lies in complete ablation of both phrenic nerves at the first operation.

I had hoped to bring out more discussion on the absorbing subject of nerve regeneration. I do not know of a case in the literature in which there have been so many cycles of deliberate removal of a motor nerve, alternating with unwelcome regeneration. It is, in truth, seldom that a motor nerve is deliberately divided; more often a divided motor nerve is sutured, with the fervent hope that functional union will occur in the due course of time.

Herniation of the Nucleus Pulposus and Hypertrophy of the Ligamentum Flavum: Diagnosis, Treatment and Result. DR. ROBERT A. GROFF.

The cases of 25 patients who had either herniation of the nucleus pulposus or hypertrophy of the ligamentum flavum verified by operation were reviewed from the standpoint of the clinical syndrome and the results of operative treatment.

In 16 of these 25 cases the lesion was attributed to trauma, whereas in the remaining cases there was no history of injury.

The character of the symptoms was aching in the lower part of the back, with unilateral or bilateral sciatic pain. Thirteen patients had pain which was constant from the onset and was aggravated at times. Nine had attacks of pain lasting several months, with intervals of comparative freedom. Three had attacks with intervals of freedom in the beginning, and then the pain became constant.

The neurologic signs varied. Diminution or absence of the achilles reflex was the most constant, being present in 14 cases. The Lasègue sign was found in 12 cases, motor weakness in 6 and sensory disturbance in 5. Five patients showed no abnormal neurologic signs.

All patients had a spinal injection of iodized poppyseed oil. In only 1 instance was the result of this examination negative and the herniated nucleus pulposus found at operation.

The location segment of the defect in these 25 cases was as follows: twelfth thoracic, 1 case; first lumbar, 1 case; second lumbar, 2 cases; third lumbar, 2 cases; fourth lumbar, 13 cases, and fifth lumbar, 5 cases.

Two cases of hypertrophy of the ligamentum flavum are included in this group; in these cases herniation of the nucleus pulposus was not present. One patient had herniation of the nucleus pulposus of two intervertebral disks (third and fourth lumbar). Laminectomy was performed in 20 cases and hemilaminectomy in 5. The follow-up statistics show excellent results in 9 cases, good results in 11, fair results in 2 and no relief in 3.

The 5 patients who were subjected to hemilaminectomy had recurrence of pain. A second operation was performed on 2 patients, with removal of the entire lamina and ligamentum flavum and introduction of an osteoperiosteal graft. They have had complete relief of pain. The remaining 3 patients had no relief from pain. With these results, the suggestion is made that all patients should have complete removal of the lamina instead of the lesser operation of hemilaminectomy.

DISCUSSION

DR. N. C. NORCROSS, San Francisco: Cases of this condition have interested me for some time, and there are a number of things about them that are not quite clear. After having done bilateral laminectomies for some time, I changed to the limited procedure of unilateral laminectomy. After this operation some of the patients convalesced satisfactorily until they again became active, at which time new symptoms appeared. These consisted of discomfort and pain radiating into the superior gluteal and inguinal regions on the side of operation. The nerve supply to these regions is considerably higher than any roots exposed at the time of operation. I have not been able to explain this phenomenon satisfactorily. In regard to the long range prognosis in these cases, I feel that certain facts should be more generally known. A patient with rupture of an intervertebral disk as the result of a minor trauma does not, in all probability, have a normal back to begin with, and it is too much to expect that he can return to heavy manual work without having further trouble. On the other hand, his condition can be tremendously improved and his disability considerably reduced. Patients who are not engaged in strenuous work should not have any significant disability after operation. In regard to duration of convalescence, I have seen repeatedly instances of what I felt was unnecessarily prolonged recovery among compensation cases. In regard to the diagnosis and investigative studies, I believe that pneumomyelograms are unsatisfactory and that even iodized oil fails at times to show a pathologic condition which proves to be present at operation. In view of this, it is my feeling that patients with a history of prolonged sciatic pain who show objective

neurologic signs, such as decreased ankle jerk, weakness of the extensor hallucis longus muscle or decrease in sensation over the lateral aspect of the calf or dorsum of the foot, should be operated on without examination with iodized oil. Spurling has reported a series of cases in which this was done. His figures compare favorably with the results of others who have used iodized oil routinely.

DR. J. C. YASKIN: The subject of backache and pain down the leg in relation to protrusion of intervertebral disk has interested me for the past two years, and I have seen about 38 verified cases. The history in cases of this condition may be either clearcut or extremely vague. There is nearly always a history of trauma, either recent or in the remote past. Such patients complain of backache and pain down the thigh. In about 50 per cent of cases the pain is so intense that the sufferer is unable to sleep. As a rule, but not always, there is a history of pain in the back. The pain is usually not in the distribution of the sciatic nerve but is referable to the irritation of the upper and lower lumbar roots. There are no pathognomonic symptoms or signs.

In the final analysis the diagnosis depends on the findings with iodized oil or some other contrast medium. In my opinion, a patient should not be subjected to study with iodized oil unless he has had the benefit of thorough-going orthopedic treatment for a prolonged period. Negative results of study with iodized oil not always exclude the existence of a protruded disk. I have 2 cases in which such studies gave negative results, but at operation a disk was found in each case and removed, with satisfactory relief. It is of diagnostic interest to note that frequently after the administration of iodized oil the backache and pain increase on the affected side.

DR. F. H. LEWY: The problem of the mechanism of pain in these cases is still unsolved. It is unlikely that the protruded disk alone causes the paroxysmal, progressive attacks of pain. Dr. Groff has operated on a number of patients with the clinical signs of a herniated nucleus pulposus in whom protrusion of the disk was not found but who were cured by removal of the corresponding ligamentum flavum. This ligament is frequently enlarged and seems to strangulate the posterior root, which appears red and swollen. Histologic examination of such a ligament shows either traumatic rupture of elastic fibrils, with scar formation in an otherwise normal ligament, or perivascular, inflammatory degeneration of elastic fibrils or diffuse disease of unknown origin. More attention should be paid to the role of the ligamentum flavum in the syndrome of herniated nucleus pulposus.

DR. B. J. ALPERS: This material represents a good deal of real diagnostic acumen. I doubt that cases of this lesion are as numerous as they appear. Have there been any cases in which the studies with iodized oil gave positive results and operation did not reveal herniation of the nucleus pulposus?

DR. MICHAEL SCOTT: Several questions have occurred to me in connection with this discussion on herniation of the nucleus pulposus and hypetrophy of the ligamentum flavum: Is there any connection between the age of the patient and the development of either one of the two conditions under discussion? By this I mean, are young persons more likely to have hypertrophy of the ligamentum flavum? Second, is air not just as useful in visualizing the pathologic lesion as iodized poppyseed oil? My associates and I have visualized these lesions with air in order to obtain good pictures; however, when using the air technic we have had to pay particular attention to the exposure and the type of film. In most instances neglect of these two factors is responsible for the failure.

DR. A. M. ORNSTEEN: I should like to ask Dr. Groff whether in his case the protein determination of the spinal fluid was of assistance in diagnosis. I am of the impression that in all these cases there is an increase in the protein content of the cerebrospinal fluid.

DR. ROBERT A. GROFF: About 48 per cent of these 25 patients showed an increase in the protein of the cerebrospinal fluid. The degree of increase was only 10 or 15 points above the normal. My feeling is that the examination is helpful

but that the diagnosis is not excluded when the figures are normal. The inaccuracy of methods for determinations of protein in the fluid must also be considered.

In reply to Dr. Alpers' question regarding cases in which herniation of the nucleus pulposus was suggested by studies with iodized oil and none was found at operation: Up to the present I have performed an exploratory operation in 6 such cases. In the last 15 cases of a present total of 40, there have been no negative results of exploration. In 1 case herniated nucleus pulposus was removed at the fifth lumbar interspace and the iodized oil studies revealed no lesion. In this series of 25 patients, 7 had definite motor and sensory signs.

In reply to Dr. Scott's question: So far as I can determine, age plays no part in the development of herniation of the nucleus pulposus or hypertrophy of the ligamentum flavum. I am well aware that air, instead of iodized oil, is a valuable means of diagnosis; however, from my experience I must say that if the results of air studies are positive, the lesion ought to be checked by injections of iodized oil. I have had 3 patients for whom air myelograms were positive and the operative observations negative.

SAMUEL B. HADDEN, M.D., *Presiding*

Regular Meeting, Nov. 22, 1940

Congenital Stenosis of the Jugular Foramens: Report of a Case. DR. TEMPLE FAY and DR. HENRY WYCIS.

Mechanical obstruction to the outflow of cranial blood may be caused by congenital stenosis of the jugular foramens.

Edwards studied autopsy material and found 50 cases in which the combined areas of the transverse and inferior petrosal sinuses varied considerably on the two sides, being larger on the right in 25 cases, larger on the left in 21 cases and equal in 4 cases.

Dr. D. B. Davis, a former fellow in neurosurgery at Temple University Hospital, reported on a roentgenographic analysis of the jugular foramens in epileptic patients. He utilized the technic for measurement devised by Dr. W. Edward Chamberlain. Of 40 epileptic patients studied, he found that the foramen was larger on the right side in 28 and larger on the left in 11. Of 10 control subjects studied, 9 had a larger jugular foramen on the right and 1 a larger foramen on the left. However, the combined areas of the jugular foramens on the two sides in the epileptic patients were found to be much smaller than those in the control subjects.

A case of bilateral congenital stenosis of the jugular foramens associated with convulsive seizures is reported.

REPORT OF CASE

History.—R. F., a girl aged 2½ years, was admitted Sept. 14, 1940 to the neurosurgical service of Dr. Temple Fay with the complaints of (1) convulsive seizures of one year's duration, (2) inability to balance herself on her feet for the past six months and (3) delay in speech and general mental development.

The patient was in usual good health until one year before admission to the hospital, at which time she had a major generalized convulsion. Salivation and nystagmoid movements of the eyes were present during the seizure. Similar attacks had occurred at irregular intervals up to the time of her admission. She was slow in learning and unresponsive to her environment. She began to speak a few words at 22 months of age. For the past six months she had been unable to balance herself on her feet. This loss of balance was gradual and was not accompanied by any noticeable weakness.

Examination.—Mental retardation was obvious. The child was unresponsive and would sit with her legs crossed, continually chewing the hem of her dress. At other times she would bury her head in a pillow and remain in such a posture

for hours. She did not speak, although she could understand commands and requests, especially at mealtime. Crying could be elicited with noxious stimuli, but only for a short time. The skull was peculiarly shaped. The external occipital protuberance was very large and prominent and seemed to overhang the base of the skull. The anteroposterior diameter of the skull was also greater than normal. There was dulness to percussion over the right parietal region. The cranial nerves were normal. Motor power was unimpaired, and muscle tone was uniformly fair. The deep tendon reflexes were normal, and no pathologic reflexes could be elicited. Coordination was normal. There was no apparent disturbance in sensation.

Laboratory Examination.—The red and white blood cell counts were normal. Urinalysis showed only a slight trace of albumin. There were 22 white cells per cubic millimeter of the cerebrospinal fluid, 38 per cent of which were polymorphonuclear, 50 per cent lymphocytes and 12 per cent monocytes. The Wassermann reaction was negative, and the colloidal gold curve was normal.

Roentgenographic Examination.—Special roentgen studies of the skull, including those of the base, were reported on by Dr. W. Edward Chamberlain as follows:

"The right jugular foramen is much smaller than normal, and the left jugular foramen is at the lower limits of normal size. Often, when one jugular foramen is smaller than normal, a compensatory enlargement of the other is visualized, but in this child the right is smaller than normal and the left is barely ample. The other foramens at the base are considered normal."

An encephalogram showed the ventricles to be asymmetrically developed, the left lateral ventricle being the larger. The third ventricle, as well as the lateral ventricles, was larger than normal. The cortical subarachnoid pathways were unduly prominent over the parietal lobe of both cerebral hemispheres. Cortical markings were seen as far posteriorly as the occipital pole, producing the appearance of a communicating type of hydrocephalus with considerable "cortical atrophy," particularly on the left side where the left lateral ventricle was larger than the right.

The rather characteristic encephalographic appearance of obstruction to escape of subarachnoid fluid into the superior sinus is shown by the widespread cortical markings extending to the occipital pole and, in our opinion, denotes obstruction to venous outflow from the skull due to congenital stenosis of the jugular foramens.

Hereditary Ataxia in Identical Twins Affecting the Cerebellum and Certain of Its Physiologically Related Structures: A Clinicopathologic Study. Dr. George Wilson and Dr. James S. Dean.

Since Marie's attempt in 1893 to distinguish a clinical entity of "parenchymatous hereditary cerebellar ataxia," an extensive literature and divergent opinions have arisen regarding the cause, the role of heredity and the pathologic relations of such a disorder. Identical twin brothers, each showing clinical symptoms conforming largely with those of Marie's hereditary cerebellar ataxia, are presented. The chief symptom presented by each patient was marked ataxia of the trunk and the upper extremities, which commenced at the ages of 33 and 34, respectively, and was followed by gradual development of dementia and euphoria, bilateral signs referable to the pyramidal tracts and, finally, optic atrophy, the course of the disease being progressive over approximately twenty years. The signs of involvement of the pyramidal tract and optic atrophy were greater on the one side in one twin and on the opposite side in the other twin. Death occurred from bronchopneumonia at the ages of 64 and 66, respectively.

The neuropathologic features presented by each patient were: widespread degeneration of the cerebellum with pronounced reduction of the Purkinje cells and considerable demyelination of the cerebellar white matter; slight to moderate lipoid degeneration of the dentate nuclei; moderate and disproportionate degeneration of the frontal cortex and its subjacent white matter; questionable slight

demyelination of each middle cerebellar peduncle; degeneration of both inferior olives and their hilar, adjacent fibers and those destined for the restiform bodies, and marked bilateral degeneration of the optic nerves (being greater on the right than on the left in 1 patient and greater on the left than on the right in the other). The absence of demonstrable demyelination in the superior cerebellar peduncles in the presence of such degeneration in the cerebellum was unexplained, but was felt to be noteworthy, as was the paucity of arteriosclerosis.

The congenital or hereditary nature of the condition was strongly suggested by (1) the fact that the twins were uniovular; (2) the approximately identical ages of onset in early life; (3) the similarity in the nature and chronologic sequence of symptoms, and (4) the approximately identical neuropathologic changes. "Mirror imagery" of identical twins was suggested by the fact that optic atrophy and pyramidal signs were predominant on one side in 1 patient and on the opposite side in the other.

The preponderance of the pathologic lesions in the cerebellum, inferior olives and frontal lobes (neokinetic structures) suggested that the underlying morbid process was a developmental defect in those motor portions of the central nervous system which are phylogenetically more recent. The onset of symptoms in later life suggested that the stresses and strains of postnatal life finally caused a congenitally "diminished reserve" to become clinically manifest.

Review of the literature and study of these cases prompted the suggestion that many of the "heredoataxias" do not represent specific clinical or pathologic entities but are fragmentary or more extensive expressions of defective embryonic development of those motor and auxiliary neural structures phylogenetically and ontogenetically more recent.

DISCUSSION

DR. HELENA E. RIGGS: In these cases there has been diffuse loss of ganglion cells in the brain stem, particularly those most highly differentiated, such as the Purkinje cells and those of the dentate nuclei and inferior olives. Both the brothers showed anomalies of the portions of the cerebral vascular tree supplying the brain stem. In 1 case the entire basilar artery was hypoplastic; in the other the branches of the basilar artery were extremely small. In this study interest has been directed to the relation of anomalies of the cerebral vascular tree to abiotrophies and chronic degenerative diseases of the nervous system. In 92 per cent of 84 cases of such conditions abnormalities of the vascular tree were apparent in the areas of greatest degeneration. This series included 20 cases of chronic degenerative basal ganglion disease, 11 cases of multiple sclerosis, 6 cases of amyotrophic lateral sclerosis, 5 cases of cerebellar ataxia, 4 cases of syringomyelia and 2 cases of diffuse sclerosis. The restriction of circulation in the anomalous field of supply is not sufficient to prevent normal development of the brain, but in middle life, with increasing general circulatory insufficiency, the blood supply to such areas is not adequate for normal function. Since circulation is impaired rather than cut off, the result is an abiotrophy, in which cells with the highest metabolic rate are affected first and most severely.

DR. JAMES S. DEAN: I appreciate Dr. Riggs's presentation of the vascular changes in these cases, and I feel it brings up an interesting question. It is true that the blood vessels (namely, the anterior cerebral and the posterior inferior cerebellar arteries) leading to the prefrontal and the medullary-cerebellar structures are normally relatively small. The cerebellum, however, was markedly reduced and grossly hypoplastic or atrophic, whichever the case may have been. In any event, the smallness of the cerebellum was more pronounced than could be explained by the slight degree of arteriosclerosis or the age of the patient. The earliest symptom was that of a cerebellar type of ataxia, which began in the early thirties in each case. This was superseded by a progressive organic type of dementia. I confess I am unable to determine "which came first" in this situation. Did the vascular hypoplasia precede and predispose to the frontal and cerebellar hypoplasia or atrophy, or did an original hypoplasia of the frontal lobes and cerebellum require a less extensive development of the vascular branches

supplying these structures? It is my opinion that in embryonic development the structural size and function of an organ predetermine the extent of the development of the vascular supply.

I regret that I was unaware of Dr. Spiller's having reported clinically to the society before my time the presence of these 2 interesting cases at the Philadelphia General Hospital. I had occasion to examine only 1 of the twins during life.

Therapy of Parkinsonism. Dr. Herbert Freed, Dr. M. D. Person and Dr. Bernard Widman.

Twenty patients with parkinsonism, which in all but 1 instance was considered of postencephalitic origin, were treated with roentgen rays. All of these patients were ill for long periods, the average duration being sixteen years, and required prolonged periods of hospitalization, which included every known form of therapy. The roentgen dosage was 100 r, given in divided doses to the full side of the head, with an average of 1,000 r over a period of three weeks. The patients were then observed for eighteen months. They were given complete neuropsychiatric examinations at two month intervals. During this period of observation 4 patients died, at intervals of two months to a year after the last roentgen treatment. Autopsy was performed on 2 of these patients, and the neuropathologic changes were particularly noted.

Most of the patients showed varying degrees of subjective improvement, which lasted at times throughout the period of observation. While this is consistent with the reports of some other observers, the suggestive effect of a new form of therapy was also considered a potent factor in influencing the patient's attitude. Only 1 patient showed significant objective improvement, characterized by lessened rigidity and tremor, sufficient to leave the hospital, after a stay of five years. In the cases in which autopsy was done, histologic examination showed advanced lesions in the basal ganglia that did not appear to be related to the roentgen treatment but which seemed too advanced to be influenced favorably by any form of therapy. It had been thought that the roentgen treatment might produce an increased blood supply to the basal ganglia and remove particularly the radiosensitive round cell exudates from diseased areas.

DISCUSSION

Dr. Joseph C. Yaskin: Do the pathologic lesions have any significance in the roentgen treatment? Was there any actual inflammatory reaction?

Dr. Helena Riggs: Dr. Freed has asked me to discuss the possible effects of treatment on the brain. It is difficult to make any positive statement on the basis of the 2 cases in which autopsy was performed. However, in these 2 cases I cannot see how any form of therapy could have improved the condition of the brain. There was widespread loss of neural elements with proliferation of fixed glia cells. The fact that there were irreversible changes in the walls of the blood vessels with collagen fibers filling the perivascular spaces precludes improvement on the basis of increased blood flow. Although it may be merely coincidence, the death of both patients from circulatory collapse and hypostatic pneumonia suggests a possible deleterious effect of roentgen treatment through its effect on the carotid sinus and the sympathetic fibers on the internal carotid vessels. While the dosage used in these cases was small, the effect of previous neural damage in cases of parkinsonism may predispose the nerve tissue to untoward effects from irradiation.

In answer to Dr. Yaskin, the small amount of perivascular round cell infiltration in these cases was considered evidence of an inflammatory reaction to tissue degeneration rather than of residual infection.

Dr. Herbert Freed: I feel that the small doses of roentgen rays would not harm the normal brain, but I must concede that in these cases the brains were not normal. The patients had no subjective complaints after the treatment. There was no headache and no disturbance of sleep.

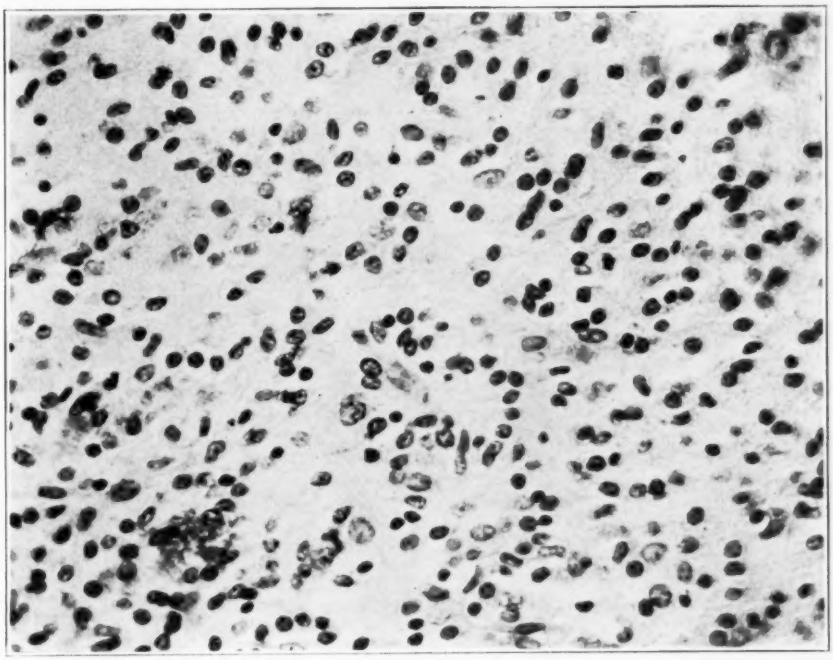
CHICAGO NEUROLOGICAL SOCIETY

HARRY PASKIND, M.D., *President, in the Chair*

Regular Meeting, Jan. 16, 1941

Experimental Production of Intracranial Tumors in the White Rat. DR. WILLIAM H. SWEET (by invitation) and DR. PERCIVAL BAILEY.

After the demonstration of the carcinogenic properties of chemical substances of the cholanthrene series, attempts were made in numerous laboratories to provoke by their use the formation of tumors of the interstitial tissues of the brain (Weil,



Glioma of the brain of a white rat. Hematoxylin and eosin stain; × 300.

Seligman and Shear, Oberling and Guérin, Bertrand and Gruner, Peers, Askanazy and Scherer). We also began such experiments in September 1937, but, before there was evidence of the development of tumor in any of our animals, Seligman and Shear (April 1938) settled the problem with a finality and wealth of detail which apparently left nothing to be desired. For this reason, and also because both of us were away from the laboratory during long periods, our material was merely collected and stored, as the animals died or were killed, to await our leisure for its detailed examination. The rather meager results of this abortive effort of ours seem to us to deserve a brief report.

Crystals of 20- methylcholanthrene (supplied us by Dr. Alexander Brunschwig) were implanted directly into the cerebrum or the cerebellum of 42 Wistar white rats of all ages, from 4 weeks to adults. In 5 of these animals tumors developed which were obvious grossly. One adult rat began to show ataxia five months after implantation of the crystals and died. Necropsy revealed an intracranial, extra-

cerebral tumor, compressing the cerebellum, which had the structure of a fibroblastoma. Another adult rat died some eight months after the implantation, and at necropsy a tumor resembling in structure a lymphosarcoma was observed to have spread throughout the leptomeninges and the ventricular system. In addition, in the oval center of the right cerebral hemisphere was a separate focus of neoplastic proliferation having all the microscopic earmarks of a glioblastoma, as it is observed in human brains. The latter tumor evidently arose from the interstitial tissue of the brain. Numerous mitoses (as can be seen in the projections) occurred in the neuroglia, at a distance from any blood vessels or other source of connective tissue cells. In addition, in 3 rats spindle cell sarcomas developed in the extracranial tissues; these were quite different in microscopic appearance from the intracranial meningeal fibroblastoma.

In a number of rats the methylcholanthrene was observed at necropsy to be encysted, with a surrounding foreign body reaction but no evidence of neoplastic formation. Microscopic examination of the other brains revealed nothing of interest, although many of the rats had survived from seven to as much as twenty-two months after implantation of the crystals.

These results seem to indicate that it is more difficult to provoke neoplastic development in the interstitial tissues of the rat than in those of the mouse by means of methylcholanthrene, at least in the strain we used. This is also true of the leptomeningeal tissue, since in a series of 36 mice in which methylcholanthrene was placed in contact with the leptomeninges, spindle cell sarcomas had already developed in 5 in less than six months and tumors would doubtless have developed in many more if we had not been obliged to kill the remaining animals at that time.

DISCUSSION

DR. ARTHUR WEIL: Dr. Bailey's skepticism in regard to the production of tumors in the brains of white rats by implantation of methylcholanthrene is justified when one compares the results with those reported by Seligman and Shear (*Am. J. Cancer* **37**:364, 1939). These authors, however, used the C_3H strain of white mice, which seems to be especially susceptible to the carcinogenic effect of methylcholanthrene. But with some patience and persistence results may be seen in the white rat, too. Recently, Dr. Greenwood showed me his preparations of methylcholanthrene tumors in the brains of white rats, made in the department of anatomy of the University of Chicago. There was no doubt that he had produced glioblastoma and fibroma of the meninges.

As early as 1938, I published a paper on the effect of dibenzanthracene on the rat brain (Experimental Production of Tumors in Brains of White Rats, *Arch. Path.* **26**:777 [Oct.] 1938). In 1 case both an epidermoid carcinoma and a glioma had been produced within the same brain. Strangely, Peers, whose efforts had been entirely without success, without studying my histologic preparations, came to the conclusion that "a direct relationship between this mass and the implanted chemical was not demonstrated" (*Am. J. Path.* **15**:26 [March] 1939), notwithstanding that the published photomicrograph in my paper (fig. 1 *A*) shows clearly the granuloma of the pia-arachnoid with the dibenzanthracene crystals in the immediate neighborhood of the glioma and of the carcinoma. More recently I observed small gliomas in the rat brain after implantation of methylcholanthrene crystals and a large glioma of the spinal cord in combination with an extradural sarcoma. (Lantern slides were demonstrated.)

DR. ROBERT GREENWOOD: This work was started about 1936. By the end of 1939, 19 rats had received injections of methylcholanthrene—in the cerebrum in 13, in the cerebellum in 5 and in the retrobulbar space in 1. In 1 rat a large glioma occupied about one third of the hemisphere and was accompanied by neurologic signs. In 4 others the tumors proved to be a fibrosarcoma, identical with those described by Dr. Bailey; in a sixth animal the tumor resembled a meningioma, and in a seventh, an adenoma. Other rats received injections of 1,2,5,6-dibenzan-

thracene and styryl 430 (2 [p-aminostyryl] 6 [p-acetylaminobenzylamino] quinoline methoacetate). Of these, granulomas developed in 2 or 3, and in 2 others there was some glial proliferation in which questionable neoplastic changes occurred.

DR. LLOYD ZIEGLER, Wauwatosa, Wis.: This interesting presentation has suggested to me two questions. Do these chemical substances produce tumors in any other parts of the body, and is there anything in the body metabolism that might tend to produce such chemical substances?

DR. R. P. MACKAY: What is the incidence, if any, of spontaneous tumors of the brain in these various strains of mice? If the incidence of susceptibility to artificially produced gliomas is the same as that to spontaneous gliomas, then the real cause of the tumors is not the irritant, but some inborn trait.

DR. PERCIVAL BAILEY: In neither the rat nor the mouse does glioma develop spontaneously; to my knowledge at least, nobody has ever described such an instance. Methylcholanthrene is not formed in the body. Although there is some correlation between the carcinogenic compounds and the sterol group of natural products, the exciting factor in the formation of glioma in the human being is unknown. The study of experimental tumor of the brain is of course in its infancy. It is obvious that a great many factors are concerned. One is undoubtedly the time factor. Gliomas develop in mice in one hundred and eighty to two hundred and ninety days; in the rat it apparently takes much longer.

Pick's Disease: Clinicopathologic Study and Report of a Case. DR. G. B. HASSIN and (by invitation) DR. DAVID LEVITIN.

This paper appears in the May issue of the ARCHIVES, page 814.

Deterioration in Epilepsy. DR. ALEX J. ARIEFF and DR. G. K. YACORZYNSKI.

Because of the many contradictory reports on deterioration in epilepsy, especially that resulting from the use of bromides, the following report is presented.

Sixty-three outclinic patients with nonorganic epilepsy, 49 of whom had received bromides for periods of from six months to five years, with the bromide content of the blood varying from 75 to 250 mg. per hundred cubic centimeters, 9 phenobarbital and 5 no sedatives, were given the Stanford-Binet intelligence test at intervals of one to three years.

In these patients bromides appeared to have no deteriorating effects, since there was no change in the intelligence quotients associated either with the amount or with the length of bromide treatment. The small number of patients under phenobarbital therapy likewise showed no deterioration.

Eight patients showed significant increases in the intelligence quotient and 7 patients significant decreases. If only progressive changes in the intelligence quotients are considered, then only 1 patient, or 1.6 per cent, showed improvement and 3 patients, or 4.8 per cent, deterioration.

On 27 additional patients with epilepsy of definite organic origin, similar tests were performed at intervals of from one to nine years. In this group there was definite deterioration with an average decrease of 6.0 points in the intelligence quotient between the time of the first and the last test. This group differed from the previous group with nonorganic epilepsy in that the initial intelligence scores were lower.

In 11 per cent of the cases of organic epilepsy there was a significant increase in the intelligence scores and in 37 per cent a decrease. These data are in contrast with those for patients with nonorganic epilepsy, among whom the number of deteriorated patients was 5 or 6 per cent.

DISCUSSION

DR. PERCIVAL BAILEY: I should like to ask what the authors mean by nonorganic epilepsy. Do they mean that it is psychogenic?

DR. R. P. MACKAY: Is there any evidence that a process of learning alters the results obtained with repeated intelligence tests on the same subject?

DR. A. J. ARIEFF: By nonorganic epilepsy I mean what every one else means, the so-called idiopathic type. We tried to eliminate the cases in which we could find some obvious cause, and those in which we could not find evidence of organic origin we put into the big storehouse of nonorganic epilepsy.

I should like to have Dr. Yacorzynski reply to Dr. Mackay's question. It requires a psychologic answer. If the patients with organic epilepsy showed deterioration in spite of the possibility of learning, the latter had little, if any, effect, as brought out by Dr. Yacorzynski. On repeated tests 35 per cent showed deterioration. If there was any chance of their learning, a higher percentage would have shown deterioration. It is known that repeated psychologic tests have little or no statistical effect on the successive scores.

DR. G. K. YACORZYNSKI: Previous studies have shown that when the Stanford-Binet test is administered at intervals of a year there is little indication that learning takes place. The patients who in our study were tested four or five times were given the test at intervals of one or more years. The fact that in the idiopathic group there is no indication of either an increase or a decrease in the intelligence quotient shows that there was no change in the score other than that which would be expected by chance. As a matter of fact, we retested some of the patients with the 1937 revision of the Stanford-Binet test, whereas the test originally used was the 1916 form. The shifts in the intelligence quotients among the persons who were consistently tested by the same scale and those of the persons who were not showed no significant differences.

Book Reviews

A Review of the Psychoneuroses at Stockbridge. By Gaylord P. Coon and Alice F. Raymond. Pp. 299. Stockbridge, Mass.: Austen Riggs Foundation, Inc., 1940.

This book is a study of the clinical records and a statistical analysis of the cases of patients treated at Stockbridge, Mass., between 1910 and 1934. The outstanding feature is an evaluation of the end results of treatment. Inasmuch as the study covers a twenty-five year period, the effect of changing forms of therapy is apparent. The report is for the most part based on clinical records, but these have been amplified by correspondence and follow-up visits. The project required three full years for completion, and the devoted and painstaking work of the authors is evidenced in this review.

The individual case reports are few, but the conclusions are based on a summary of 1,060 cases out of a total of 5,300. The report is rich in details which illustrate the dynamic interrelations of personality factors. In general, the cases represented psychoneurotic conditions, for Dr. Riggs's practice for many years was confined to patients with disorders of this type. When the Riggs Associates was formed in 1937, it carried on the work of the Austen Riggs Foundation, which had been established in 1917 for the service of patients who were unable to pay the usual fees of private psychiatrists. One of its chief aims was to avoid in care of the patients the appearance of institutional life and of nurses in uniform; locked doors and barred windows were notable for their absence.

Miss Raymond and Dr. Coon describe early in the book the limitations of psychoneurotic patients and of the classification of "psychoneurosis." They discuss the difficulties of differential diagnosis and the method of treatment at Stockbridge. There, the feeling has been strong that (*a*) a balance in the day's activity, (*b*) the habit of accepting reality, (*c*) the habit of living in the present and (*d*) a consistent purpose expressed in useful work are ideals which are of maximum importance in directing a patient to the resumption of an integrated behavior pattern.

There are 92 formulations of cases, and among them the following types of patients stand out:

(1) "The overly ambitious, conscientious, dynamic, energetic persons who drive at fever pitch toward material goals"; (2) "the essentially immature, overly dependent, impractical people . . . ill-equipped to meet ordinary . . . life"; (3) "the emotionally immature married women of middle age now deprived of the affection and solicitude of their husbands by death and who feel lonely and insecure," and (4) "the immature married woman who feels extreme guilt because of extramarital affairs."

Reeducation at Stockbridge appears to have a place midway between the so-called persuasive method of Dubois and the psychobiologic approach of Adolf Meyer. The book is well written and edited and testifies to the perception and analytic skill of the authors.

Psychiatric Social Work. By Lois Meredith French. Price $2.25. Pp. 344. New York: Commonwealth Fund, 1940.

This balanced and provocative study, begun with the aid of a grant from the Commonwealth Fund, was conducted under the supervision of the Advisory Committee on Standards of the American Association of Psychiatric Social Workers.

The author traces the history of psychiatric social work from its early beginnings, noting the organization of the American Association of Psychiatric Social Workers twenty-five years ago, the influences on psychiatry of the first World War, the development of child guidance clinics and services and their consequent effects

on psychiatric social work. Owing to the growing body of knowledge developed in psychiatric social work, its concepts have permeated other fields, such as education and public health. Because of the bearing of psychiatric social work on "psychiatry, psychology, mental hygiene and other fields of social work and because it was influenced strongly by the developments in other fields . . . conflicting issues and uneven growth" have ensued.

The study is timely, for it reclarifies the objectives in psychiatric social work and reaffirms its province as that of social work practiced in relation to psychiatry though psychiatric social workers have entered other fields of social service and have brought to them added equipment in dealing with maladjusted persons. Order in thinking in relation to psychiatric social problems is established and clarity attained when "once the basis for definition of the field is shifted from the activities of workers to the basic criterion, which is affiliation with psychiatric services."

The chapters on vocational trends, opportunities for placement and salaries will afford orientation to the student considering entrance into the field. The chapters on "Social Work in Relation to Psychiatry," the place of psychiatric social work in "Hospitals and Clinics" and in "Mental Hygiene Education" and "Some Trends in Treatment" will serve as excellent means of reorientation to the professional psychiatric workers engaged in this field who have been and are participating in its development To them the study suggests projects and issues that should be further pursued. To physicians employed in psychiatric hospitals and clinics the book will give an understanding of the background, experience and equipment of these colleagues who contribute to the treatment of their patients. They will read of the concern of this specialty with the advances made in psychiatric knowledge and practice and will be reminded of the constant aim of these specialists to keep aware of "the delicate relationships existing between physical and mental states" and of their realization that the "developing responsibility for social treatment should be continually checked against medical and psychiatric practice." The book states that the essence of psychiatric social work lies "in the continued contribution of . . . [its] experience to the practice of psychiatry and the continued utilization in the practice of social work of knowledge and experience gained in psychiatric fields."

INDEX TO VOLUME 45

The asterisk (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.